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Original Research

A nationwide case–control study on cardiovascular and respiratory-related disorders in patients with gambling disorder in Sweden

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A B S T R A C T

Objectives: We aimed to examine potential relationships and gender differences between cardiovascular disease (CVD), diabetes, obesity, respiratory-related disorders, and gambling disorder (GD). We hypothesized that (1) GD patients would be more likely than controls to have CVD, diabetes, obesity, and respiratory-related diseases; and (2) females with GD would be more likely than men with GD to have CVD, diabetes, obesity, and respiratory-related diseases.
Study design: National retrospective case–control study.
Methods: We used data from the Swedish National Board of Health and Welfare between 2005 and 2019. A total of 10,766 patients were included, and 3592 of them had GD. Every GD patient was matched with two age- and gender-matched controls. Patient data, including the history of medical diagnoses, were extracted. Descriptive statistics, Chi-squared and Fisher's exact tests were used to compare GD patients and controls.
Results: GD patients had a higher prevalence of CVD and respiratory-related disorders than controls. Diabetes rates were 5% for GD patients and 2% for controls; CVD (18% vs 12%); respiratory-related disease (7% vs 4%); and obesity (7% vs 3%). Women with a diagnosis of GD have a higher prevalence of obesity and somatic comorbidities other than diabetes compared to men.
Conclusions: This is the largest case–control study conducted to date showing GD patients have a higher prevalence of CVD, diabetes, obesity, and respiratory-related disorders than controls. Women with GD appear to be more susceptible than men to CVD, obesity, and respiratory-related disorders; however, this may be partially explained by differences in help-seeking behavior. Thus, our findings highlight the importance of early identification of GD patients who may also have somatic conditions requiring treatment. This can be accomplished by implementing a screening program for GD, CVD, diabetes, obesity, and respiratory-related disorders, and by including healthy lifestyle management strategies.

Introduction

According to the DSM-5 (The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition), gambling disorder (GD) is a psychiatric condition classified as an addictive disorder.[1] Approximately 0.6% of the adult population in Sweden has GD, while another 3.6% are at risk.[2] In Norway, 1.4% of the adult population have problem gambling, while in other European countries, it

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ranges between 0.12% and 3.4%.[3] Worldwide, the prevalence of problem gambling is estimated to range from 0.5% to 7.6%.[4] A Swedish population study found that approximately 32% of men and 21% of women aged 16 to 84 years had gambled in the previous month. Adult gamblers aged 45–84 years are considered the most active, with approximately 34% engaging in regular gambling.[5] However, problem gambling remains most prevalent among Swedish younger adults aged 25–44 years, being 1.9% of the population.[2]

Only up to 20% of patients diagnosed globally with GD seek help for their gambling problems.[6] Hofmarcher et al. found that, in Sweden, only 10% of problem gamblers sought treatment.[7] Håkansson et al. demonstrated that only 20% of patients seeking GD treatment in Sweden are women, and Miller et al. examined clinical differences in GD treatment-seeking Swedish men and women.[8,9] Men seeking treatment were found to be five years younger than women, to have begun gambling 10 years earlier, and to have exhibited problematic gaming behavior for two years longer. Women also developed GD faster than men, despite having gambled for a shorter period. In addition, Syvertsen et al. showed that women who played electronic gaming machines progressed to high-risk gambling faster compared to men.[3]

Psychiatric comorbidities are common and well-studied in patients with GD.[10–13] According to a large national register study conducted in Sweden, 73% had a comorbid diagnosis in addition to GD, with anxiety and affective disorders among the most prevalent. Furthermore, they reported that women are more likely than men to have psychiatric comorbidities such as depression and anxiety. However, in their study, no gender differences were found in relation to substance use disorders.[14]

Gambling may predate and contribute to the development of physical illnesses such as cardiovascular disease (CVD), diabetes, obesity, and respiratory-related diseases. Butler et al. reported that those with problem gambling had higher odds of a poor diet, low physical exercise, and poor general health compared to non-problem gamblers.[15] The reason behind this could be that gamblers, especially online gambling, lack time for physical activity and therefore develop poorer somatic health over time compared to non-gamblers. Pathophysiological changes, such as an increased heart rate and higher levels of noradrenergic metabolites, could also be a potential explanation for the association between GD and CVD.[16,17] In addition, Grant and Potenza demonstrated that patients with GD have elevated anxiety levels.[18] Different confounding risk factors, including lipid status, hypertension, and tobacco use, may also account for the association between GD and CVD.[19] One study by Potenza et al. reported that the stress associated with gambling wins and losses may worsen cardiovascular conditions.[20] Previous studies have also reported associations between GD, CVD, and liver diseases.[19,21] Black et al. showed in their study that GD patients were more likely to be obese than controls (49% vs 28%, $P = .004$). Furthermore, patients with GD also had a higher prevalence of asthma/chronic lung disease (18% vs 10%, $P = .099$). However, no differences were found between GD group and controls regarding diabetes (7% vs 8%, $P = .693$).[22] While extant research has assessed psychiatric comorbidities in GD patients, there is a dearth of studies examining somatic health comorbidities such as CVD, diabetes, obesity, and respiratory-related diseases, and their relationship with GD. In addition, there are no studies comparing men and women with GD with respect to their somatic health.

The aim of this case–control study was to examine the association between CVD, diabetes, obesity, respiratory-related disorders, and lifetime GD. In addition, gender differences in somatic health in GD patients were investigated. We hypothesized that (1) GD patients would be more likely than controls to have CVD, diabetes, obesity, and respiratory-related diseases; and (2) females with GD would be more likely than men with GD to have CVD, diabetes, obesity, and respiratory-related diseases.[23]

Methods

Participants and recruitment procedure

This was a retrospective nationwide case–control study based on National Patient Register data retrieved from the Swedish National Board of Health and Welfare. The data retrieved included all patients over the age of 18 years with a diagnosis of GD in Swedish specialized healthcare (ICD-10 code F63.0, also known as 'pathological gambling') at any time between 2005 and 2019. Two gender- and age-matched control subjects were randomly selected from the general population using data from the Statistics Sweden population register for each patient with GD. In total, 11,067 patients were retrieved and assessed for eligibility from the registries. Patients in the control group who had a history of GD were not eligible for this study. After exclusion, the final sample consisted of 10,776 patients, of whom 3592 had a GD diagnosis, as shown in Fig. 1.

Measures

The physician records the diagnosis as an ICD-code in the patient's medical record. All ICD-codes from patients will be transferred automatically to the system. These ICD-codes can then be extracted from the National Patient Register based on inpatient and outpatient visits and used for research purposes. Based on these ICD-codes, the primary variables of this study are measured. CVD included hypertension diseases (ICD-10 codes I10–I15), ischemic heart diseases (I20–I25), diseases within lung circulation (I26–I28), other forms of heart diseases (I30–I52), cerebrovascular diseases (I60–I69), arterial diseases (I70–I79), and venous diseases (I80–I89). Respiratory-related diseases included the ICD-codes J40–J47. Furthermore, diabetes and obesity were defined as ICD-10 codes E10–E14 and E66, respectively.

Statistical analysis

All collected data were organized and analyzed in SPSS Statistics Version 28. The prevalence of CVD and respiratory-related disorders was compared between patients with GD and controls, as well as between genders, using Chi-squared and Fisher's exact tests. *P*-values <.05 were considered statistically significant.

Ethics

This study was approved by the Regional Ethical Review Board of Lund University (2019-01559) prior to its initiation and was conducted in accordance with the Declaration of Helsinki's ethical principles. The anonymity of patients was ensured by encoding data retrieved from the Swedish National Board of Health and Welfare.

Results

The present study included a total of 10,776 patients. The GD group comprised 2791 men (78%) and 801 women (22%) with a median age of 35 and 40 years, respectively, whereas the control group comprised 5581 men (78%) and 1603 women (22%) with a median age of 35 and 40 years, respectively (Table 1).

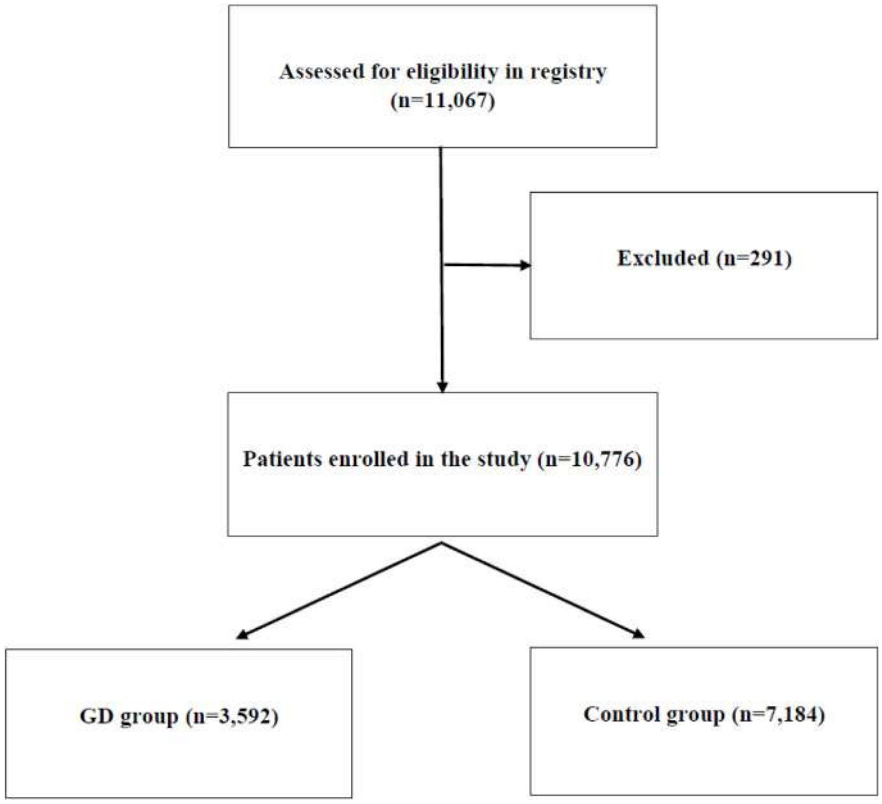

Fig. 1. Overview of the patient selection process.

Comparison between GD group and control group

As shown in Table 1, all CVD and respiratory-related disorders were significantly more prevalent in the GD group than in the control group. In the GD group, the prevalence of diabetes was three percent higher than in the control group, 5% vs 2%, respectively. Moreover, 18% of GD patients had CVD, compared to 12% of the control group. The prevalence of respiratory-related disease was greater in the GD group than in the control group. Accordingly, the prevalence of obesity was greater in the GD group than in the control group, 7% vs 3%, respectively.

Table 1
Characteristics and proportions of CVD and respiratory-related disorders at baseline for gambling disorder group (GD; F63.0) and control group between 2005 and 2019.

	GD group % (N)	Control group % (N)	*P*-value
Total	33 (3592)	67 (7184)	
Age (CI 95%, SD)	36 yrs (36–37, 12)	36 yrs (36–37, 12)	
Gender			
Male	78 (2791)	78 (5581)	.987
Female	22 (801)	22 (1603)	
CVD	18 (647)	12 (868)	***
Diabetes	5 (184)	2 (153)	***
Obesity	7 (239)	3 (200)	***
Respiratory-related diseases	7 (266)	4 (283)	***

*$P < .05$, **$P < .01$, ***$P < .001$.
CVD consisted of hypertension diseases (ICD-10 codes I10–I15), ischemic heart diseases (I20–I25), diseases within lung circulation (I26–I28), other forms of heart diseases (I30–I52), cerebrovascular diseases (I60–I69), arterial diseases (I70–I79), and venous diseases (I80–I89). Respiratory-related diseases included the ICD-codes J40–J47. Furthermore, diabetes and obesity were defined as ICD-10 codes E10–E14 and E66, respectively.

Comparison between genders in GD group and control group

In both the GD group and the control group, the prevalence of CVD and respiratory-related diseases, as well as obesity, was higher among women (Table 2). In contrast, there were no differences in the prevalence of diabetes between the two groups based on gender.

Discussion

The aim of this study was to compare CVD, diabetes, obesity, and respiratory-related disorders in GD patients and age- and gender-matched controls. This study contributes to a novel understanding of the prevalence of somatic comorbidities and obesity among patients with GDs, a topic that has received considerably less attention than alcohol or other substance use disorders. In addition, the relationship between GD and CVD, diabetes, obesity, and respiratory-related disorders, as well as gender differences, were investigated for the first time in the largest case–control study conducted to date.

As hypothesized, patients with GD had a higher prevalence of CVD, diabetes, obesity, and respiratory-related disorders compared to controls of the same age and gender from the general population. These results are consistent with those of previous research on the somatic health of gamblers, which found that pathological gamblers have a high prevalence of cardiovascular symptoms and conditions, with expected hypothesis of health worsening later in life, as found in other psychiatric disorders.[19–21,24,25] Black et al. explained that pathological gamblers are more likely to make poorer health-related lifestyle choices such as smoking, avoiding exercise, increasing food consumption, and eating junk food containing high levels of saturated fats and sugars, which could contribute to the development of somatic diseases such as CVD,

Table 2
Proportion of men's and women's CVD and respiratory-related disorders in the gambling disorder group (GD; F63.0) and control group between 2005 and 2019.

	GD group			Control group		
	Men % (N)	Women % (N)	*P*-value	Men % (N)	Women % (N)	*P*-value
Total	78 (2791)	22 (801)		78 (5581)	22 (1603)	
Age	35 yrs	40 yrs		35 yrs	40 yrs	
(CI 95%, SD)	(35–36, 11)	(40–41, 12)		(35–35, 11)	(40–41, 12)	
CVD	17 (466)	23 (181)	***	11 (612)	16 (256)	***
Diabetes	5 (134)	6 (50)	.103	2 (113)	3 (40)	.250
Obesity	4 (116)	15 (123)	***	2 (83)	7 (117)	***
Respiratory-related diseases	6 (165)	13 (101)	***	4 (204)	5 (79)	*

*$P < .05$, **$P < .01$, ***$P < .001$.
CVD consisted of hypertension diseases (ICD-10 codes I10–I15), ischemic heart diseases (I20–I25), diseases within lung circulation (I26–I28), other forms of heart diseases (I30–I52), cerebrovascular diseases (I60–I69), arterial diseases (I70–I79), and venous diseases (I80–I89). Respiratory-related diseases included the ICD-codes J40–J47. Furthermore, diabetes and obesity were defined as ICD-10 codes E10–E14 and E66, respectively.

diabetes, obesity, and respiratory-related disorders.[22] We also hypothesized that women would be more likely than men to have more CVD, diabetes, obesity, and respiratory-related disorders. This result is partly in concordance with previous studies, where it was found that whereas the coronary heart disease is higher in males, the CVD is higher in females, in the specific studied age range.[23,26] However, Nordstrom et al. found that the prevalence of type 2 diabetes was significantly higher in men than in women (14.6% vs 9.1%, $P < .001$).[27] In addition, Cooper et al. found that women have a higher prevalence of obesity than men worldwide (15% vs 11%).[28] Respiratory-related diseases such as asthma and COPD are more common in adult women than men.[29] As far as we are aware, no previous research has investigated the differences between genders in terms of GD and somatic health. However, studies on the differences in psychiatric disorders between men and women with GD have revealed that women have a higher risk of having a psychiatric disorder in conjunction with GD, but also more abnormal eating behavior (food addiction [FA]), and consequent increase body mass index (BMI), to cope with negative emotions.[12,30,31] The presence of FA in female GD (18.8% of cases) has been found to be associated with more gambling symptomatology, greater general psychopathology, more dysfunctional personality traits, less capacity to deal with emotions, and higher BMI.[30,32]

Our study highlights that little is known about the association between CVD, diabetes, obesity, and respiratory-related disorders in patients with GD. Moreover, our results indicate that, like psychiatric comorbidities, somatic comorbidities are more prevalent in GD patients compared to controls and in women compared to men, as the case of other psychiatric disorders.[25,33–35] This implies the need for health and social care professionals to early identify patients with GD who may additionally have somatic comorbidities that may need attention currently and later in life, with additional health and socio-economic burden. At this point in our knowledge, we believe that the implementation of a screening protocol could aid clinicians in the early detection of somatic conditions requiring further treatment and/or preventive interventions in patients with problem gambling or GD, in order to improve CVD, diabetes, obesity, and respiratory-related diseases, and introducing healthy lifestyles, nutritional advice, and management of sedentary behavior.[36] In addition, women appear to be more susceptible than men to psychiatric comorbidities and should therefore not be neglected and given special emphasis.

The present study is not without its limitations. One of the limitations of this study is that the data in the register was precollected and is based on ICD codes, which are registered diagnoses by health care providers and not the researcher. Moreover, register data occasionally lack essential information, such as information not reported to the register regarding diagnosis, and as a result, crucial information may be missing. Males and females approach assistance-seeking differently, which is another factor to consider. Women are more likely to seek help for mental health issues, according to previous research, and somatic symptoms and pathological gambling are no exception, which may explain why the prevalence of somatic comorbidities is lower in males than in females, as demonstrated by our findings.[37–39] A limitation of the study is that some of the patients are in the younger age range or have had their GD diagnosis for a short period of time; as a result, they have not had time to develop somatic conditions such as CVD or obesity and are therefore considered to be somatically healthy. Even though each GD patient in our study had two age- and gender-matched controls, we did not perform a matched analysis on the GD patients and their respective controls. This could have potentially introduced confounding variables into the study design and should have been accounted for in a matched analysis.

This study's inclusion of a large number of patients is one of its strengths. The register of individuals with GD used in this study is unique in that it includes all Swedish patients with a GD diagnosis. In addition, the inclusion of two controls of the same age and gender as the individual with GD is a strength.

Conclusions

CVD, diabetes, obesity, and respiratory-related disorders were more prevalent in GD patients than in the general population. The prevalence of somatic comorbidities and obesity is higher in women than in men. There were no differences in the prevalence of diabetes between two groups based on gender. This necessitates that health and social care professionals play a crucial role in identifying patients with GD who may also have somatic comorbidities requiring treatment or prevention. However, additional research is required to verify these results.

Author statements

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Ethical approval

This study was approved by the Regional Ethical Review Board of Lund University (2019-01559) prior to its initiation and was conducted in accordance with the Declaration of Helsinki's ethical principles. The anonymity of patients was ensured by encoding data retrieved from the Swedish National Board of Health and Welfare.

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Competing interests

Håkansson is a professor at Lund University, and his position at this university is financially supported by AB Svenska Spel, the state-owned gambling operator of Sweden. Also, he has obtained research funding from the independent research council of Svenska Spel, as well as from the corresponding research council of the state-owned Swedish alcohol monopoly, Systembolaget. FFA and SJM have received consultancy honoraria from Novo Nordisk and FFA editorial honoraria as EIC from Wiley. The remaining authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results. No specific funding was required for the conduct of the present study.

Author contributions

The authors confirm contribution to the paper as follows: study conception and design: YAR and AH; data collection: YAR; analysis and interpretation of results: YAR, FFA, SJM and AH; draft manuscript preparation: YAR. All authors reviewed the results and approved the final version of the manuscript.

References

1. Grant JE, Chamberlain SR. Expanding the definition of addiction: DSM-5 vs. ICD-11. *CNS Spectr* 2016;**21**:300–3.
2. Sweden PHAo. *Tabellsammanställning för Swelogs befolkningsstudie 2018. Table compilation for Swelog's population study 2018*. Public Health Agency of Sweden; 2021 [cited 2022 26 November]; Available from: https://www.folkhalsomyndigheten.se/contentassets/bbb42383175f41caa548975a4e3b92ea/tabellsammanstallning-swelogs-befolksningsstudie-2018.pdf.
3. Syvertsen A, Leino T, Pallesen S, Smith ORF, Mentzoni RA, Erevik EK. Telescoping and gender differences in high-risk gambling: loss limit behavior in a population of electronic gaming machine players. *Psychol Addict Behav* 2023;**37**:499–508.
4. Williams RJ, Volberg RA, Stevens RMG. The population prevalence of problem gambling: methodological influences, standardized rates, jurisdictional differences, and worldwide trends. *Report prepared for the Ontario Problem Gambling Research Centre and the Ontario Ministry of Health and Long Term Care* 2012 [cited 2023 27 July]; Available from: https://hdl.handle.net/10133/3068.
5. Sweden PHAo. *Tabellsammanställning för Swelogs prevalensstudie 2015. Table compilation for Swelog's prevalence study 2015*. Public Health Agency of Sweden; 2016 [cited 2022 26 November]; Available from: https://www.folkhalsomyndigheten.se/globalassets/livsvillkor-levnadsvanor/andts/spel/swelogs/tabellsammanstallning-swelogs-prevalensstudie-2015.pdf.
6. Bijker R, Booth N, Merkouris SS, Dowling NA, Rodda SN. Global prevalence of help-seeking for problem gambling: a systematic review and meta-analysis. *Addiction* 2022;**117**:2972–85.
7. Hofmarcher T, Romild U, Spångberg J, Persson U, Håkansson A. The societal costs of problem gambling in Sweden. *BMC Publ Health* 2020;**20**:1921.
8. Håkansson A, Mårdhed E, Zaar M. Who seeks treatment when medicine opens the door to pathological gambling patients-psychiatric comorbidity and heavy predominance of online gambling. *Front Psychiatr* 2017;**8**:255.
9. Miller L, Mide M, Arvidson E, Söderpalm Gordh A. Clinical differences between men and women in a Swedish treatment-seeking population with gambling disorder. *Front Psychiatr* 2022;**13**:1054236.
10. Granero R, Fernández-Aranda F, Pino-Gutierrez AD, Etxandi M, Baenas I, Gómez-Peña M, et al. The prevalence and features of schizophrenia among individuals with gambling disorder. *J Psychiatr Res* 2021;**136**:374–83.
11. Jiménez-Murcia S, Granero Pérez R, Fernández-Aranda F, Alvarez Moya E, Aymamí MN, Gómez-Peña M, et al. Comorbidity in pathological gambling: clinical variables, personality and treatment response. *Rev Psiquiatía Salud Ment* 2009;**2**:178–89.
12. Lemón L, Fernández-Aranda F, Jiménez-Murcia S, Håkansson A. Eating disorder in gambling disorder: a group with increased psychopathology. *J Behav Addict* 2021;**10**:540–5.
13. Vintró-Alcaraz C, Mestre-Bach G, Granero R, Caravaca E, Gómez-Peña M, Moragas L, et al. Exploring the association between gambling-related offenses, substance use, psychiatric comorbidities, and treatment outcome. *J Clin Med* 2022:11.
14. Håkansson A, Karlsson A, Widinghoff C. Primary and secondary diagnoses of gambling disorder and psychiatric comorbidity in the Swedish health care system-A nationwide register study. *Front Psychiatr* 2018;**9**:426.
15. Butler N, Quigg Z, Bates R, Sayle M, Ewart H. Gambling with your health: associations between gambling problem severity and health risk behaviours, health and wellbeing. *J Gambl Stud* 2020;**36**:527–38.
16. Meyer G, Hauffa BP, Schedlowski M, Pawlak C, Stadler MA, Exton MS. Casino gambling increases heart rate and salivary cortisol in regular gamblers. *Biol Psychiatr* 2000;**48**:948–53.
17. Roy A, Adinoff B, Roehrich L, Lamparski D, Custer R, Lorenz V, et al. Pathological gambling. A psychobiological study. *Arch Gen Psychiatr* 1988;**45**:369–73.
18. Grant JE, Potenza MN. Escitalopram treatment of pathological gambling with co-occurring anxiety: an open-label pilot study with double-blind discontinuation. *Int Clin Psychopharmacol* 2006;**21**:203–9.
19. Germain C, Vahanian A, Basquin A, Richoux-Benhaim C, Embouazza H, Lejoyeux M. Brief report: coronary heart disease: an unknown association to pathological gambling. *Front Psychiatr* 2011;**2**:11.
20. Potenza MN, Fiellin DA, Heninger GR, Rounsaville BJ, Mazure CM. Gambling: an addictive behavior with health and primary care implications. *J Gen Intern Med* 2002;**17**:721–32.
21. Morasco BJ, Pietrzak RH, Blanco C, Grant BF, Hasin D, Petry NM. Health problems and medical utilization associated with gambling disorders: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Psychosom Med* 2006;**68**:976–84.
22. Black DW, Shaw M, McCormick B, Allen J. Pathological gambling: relationship to obesity, self-reported chronic medical conditions, poor lifestyle choices, and impaired quality of life. *Compr Psychiatr* 2013;**54**:97–104.
23. Mosca L, Barrett-Connor E, Wenger NK. Sex/gender differences in cardiovascular disease prevention: what a difference a decade makes. *Circulation* 2011;**124**:2145–54.
24. Erickson L, Molina CA, Ladd GT, Pietrzak RH, Petry NM. Problem and pathological gambling are associated with poorer mental and physical health in older adults. *Int J Geriatr Psychiatr* 2005;**20**:754–9.
25. Vintró-Alcaraz C, Baenas I, Lozano-Madrid M, Granero R, Ruiz-Canela M, Babio N, et al. Psychological and metabolic risk factors in older adults with a previous history of eating disorder: a cross-sectional study from the Predimed-Plus study. *Eur Eat Disord Rev* 2021;**29**:575–87.
26. O'Neil A, Scovelle AJ, Milner AJ, Kavanagh A. Gender/sex as a social determinant of cardiovascular risk. *Circulation* 2018;**137**:854–64.
27. Nordström A, Hadrévi J, Olsson T, Franks PW, Nordström P. Higher prevalence of type 2 diabetes in men than in women is associated with differences in visceral fat mass. *J Clin Endocrinol Metab* 2016;**101**:3740–6.
28. Cooper AJ, Gupta SR, Moustafa AF, Chao AM. Sex/gender differences in obesity prevalence, comorbidities, and treatment. *Curr Obes Rep* 2021;**10**:458–66.
29. Silveyra P, Fuentes N, Bauza DER. Sex and gender differences in lung disease. *Adv Exp Med Biol* 2021;**1304**:227–58.
30. Etxandi M, Baenas I, Munguía L, Mestre-Bach G, Granero R, Gómez-Peña M, et al. Clinical features of gambling disorder patients with and without food addiction: gender-related considerations. *J Gambl Stud* 2022;**38**:843–62.
31. Larsson L, Håkansson A. Mental illness and socio-economic situation of women and men diagnosed with gambling disorder (GD) in Sweden - nationwide case-control study. *PLoS One* 2022;**17**:e0274064.
32. Jiménez-Murcia S, Granero R, Wolz I, Baño M, Mestre-Bach G, Steward T, et al. Food addiction in gambling disorder: frequency and clinical outcomes. *Front Psychol* 2017;**8**:473.
33. Rosenbaum S, Stubbs B, Ward PB, Steel Z, Lederman O, Vancampfort D. The prevalence and risk of metabolic syndrome and its components among people with posttraumatic stress disorder: a systematic review and meta-analysis. *Metabolism* 2015;**64**:926–33.
34. Van der Kooy K, van Hout H, Marwijk H, Marten H, Stehouwer C, Beekman A. Depression and the risk for cardiovascular diseases: systematic review and meta analysis. *Int J Geriatr Psychiatr* 2007;**22**:613–26.
35. Vancampfort D, Hallgren M, Mugisha J, De Hert M, Probst M, Monsieur D, et al. The prevalence of metabolic syndrome in alcohol use disorders: a systematic review and meta-analysis. *Alcohol Alcohol* 2016;**51**:515–21.

36. Gierisch JM, Nieuwsma JA, Bradford DW, Wilder CM, Mann-Wrobel MC, McBroom AJ, et al. Pharmacologic and behavioral interventions to improve cardiovascular risk factors in adults with serious mental illness: a systematic review and meta-analysis. *J Clin Psychiatry* 2014;**75**:e424–40.
37. Barsky AJ, Peekna HM, Borus JF. Somatic symptom reporting in women and men. *J Gen Intern Med* 2001;**16**:266–75.
38. Oliver MI, Pearson N, Coe N, Gunnell D. Help-seeking behaviour in men and women with common mental health problems: cross-sectional study. *Br J Psychiatry* 2005;**186**:297–301.
39. Slutske WS, Blaszczynski A, Martin NG. Sex differences in the rates of recovery, treatment-seeking, and natural recovery in pathological gambling: results from an Australian community-based twin survey. *Twin Res Hum Genet* 2009;**12**:425–32.

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Review Paper

Cold indoor temperatures and their association with health and well-being: a systematic literature review

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A B S T R A C T

Objective: The study aimed to identify, appraise and update evidence on the association between cold temperatures (i.e. <18°C) within homes (i.e. dwellings) and health and well-being outcomes.
Study design: This study was a systematic review.
Methods: Seven databases (MEDLINE, Embase, Cochrane Database of Systematic Reviews, CINAHL, APA PsycInfo, Applied Social Sciences Index and Abstracts, Coronavirus Research Database) were searched for studies published between 2014 and 2022, which explored the association between cold indoor temperatures and health and well-being outcomes. Studies were limited to those conducted in temperate and colder climates due to the increased risk of morbidity and mortality during winter in those climatic zones. Studies were independently quality assessed using the Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies.
Results: Of 1209 studies, 20 were included for review. Study outcomes included cardiovascular (blood pressure, electrocardiogram abnormalities, blood platelet count), respiratory (chronic obstructive pulmonary disease symptoms, respiratory viral infection), sleep, physical performance and general health. Seventeen studies found exposure to cold indoor temperatures was associated with negative effects on health outcomes studied. Older individuals and those with chronic health problems were found to be more vulnerable to negative health outcomes.
Conclusion: Evidence suggests that indoor temperatures <18°C are associated with negative health effects. However, the evidence is insufficient to allow clear conclusions regarding outcomes from specific temperature thresholds for different population groups. Significant gaps in the current evidence base are identified, including research on the impacts of cold indoor temperatures on mental health and well-being, studies involving young children, and the long-term health effects of cold indoor temperatures.

Introduction

Indoor cold exposure, cold conditions, and cold housing are common terminology used to describe cold indoor temperatures in homes (i.e. dwellings). In the present review, the terminology 'cold indoor temperatures' has been used for consistency hereafter. International evidence suggests that living in a cold home (i.e. dwelling) may contribute to a range of negative health outcomes,[1–3] including poor respiratory[3–6] and cardiovascular health,[3,7] mental illness (e.g. depression and anxiety),[2] loneliness, and social isolation[8,9] and a greater prevalence of falls.[8] Certain population groups (e.g. those of young and old age or individuals living with long-term health conditions or disability) are thought to be especially vulnerable to experiencing such outcomes.[6]

A 2016 systematic review of the impacts of cold indoor temperatures on health identified 20 studies (covering 1973 to 2014) and found negative outcomes to cardiovascular and respiratory health and to thermal comfort.[3] It also found strong evidence that homes below 18°C had a harmful effect on health but insufficient evidence to support a previously recommended minimum threshold of 21°C in living rooms.[3,10] Accordingly, and due to the wider health and well-being impacts associated with fuel poverty and the increased carbon emissions from heating homes to higher

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temperatures, the review concluded that a minimum indoor temperature of 18°C was appropriate.

Since publication of the systematic review in 2016, the UK Health Security Agency recommends a single minimum indoor temperature of 18°C.[3,11] Similarly, the World Health Organization recommends a minimum indoor temperature of 18°C for general populations during cold seasons in temperate and colder climates, but that a higher minimum temperature may be necessary for vulnerable groups, including children, the elderly and those with chronic illness.[12–14] Despite minimum indoor temperature recommendations for homes being largely consistent, the 2016 review acknowledged the need for further research to understand the relationship between behaviour, vulnerability to cold and potential risks to health in both the short term and long term.[3] To address this gap, this review aimed to identify evidence on the association between cold indoor temperatures and health and well-being published since the studies identified in the 2016 systematic review,[3] with the review expanded to include social outcomes, studies using secondary data and intervention studies.

Rising global energy prices since the latter half of 2021 have negatively affected the affordability of heating a home and have increased levels of fuel poverty, exposing more people to cold indoor temperatures.[15–17] The rising cost of energy and fuel poverty, alongside recovery from the COVID-19 pandemic and heightened awareness of climate change are all factors that may influence a household's vulnerability to living in a cold home. These current challenges exacerbate the need to further understand the impact of cold indoor temperatures on health and well-being and to help determine if temperature recommendations for homes are appropriate and, if so, at what threshold.

As such, the present review aimed to identify, appraise and update the evidence on the association between cold indoor temperatures (i.e. <18°C) and health and well-being.

Methods

Search strategy and selection criteria

Seven electronic databases (APA PsycInfo, Applied Social Sciences Index and Abstracts, Cochrane Database of Systematic Reviews, the Coronavirus Research Database, Cumulative Index to Nursing and Allied Health, Embase and MEDLINE) were searched for studies published between 1 February 2014 and 17 February 2022, which explored associations between cold indoor temperatures and health and well-being. Search terms are presented in Table 1. The search strategy expanded on that used in a previous systematic review[3] to include social outcomes, secondary data analysis and intervention studies. Database searches were supplemented through manual searching and expert consultation. Included studies met the following criteria: human subjects of all ages, measurement of specific temperatures or thresholds or energy efficiency measures/interventions (e.g. insulation or heating systems), all health and well-being outcomes, including social effects (e.g. loneliness and isolation) except sport and exercise performance, and published in the English language. Evidence synthesis (e.g. systematic review, meta-analysis), commentary/editorial, ideas and opinion pieces, studies in tropical, subtropical or arctic climates, and studies using extreme cold exposure (<5°C), overheating or outdoor temperatures were excluded. After the removal of duplicates, two reviewers (H.J. and B.G.) retrieved and independently screened titles and abstracts, then full text articles, with conflicts over inclusion resolved through discussion.

Table 1
The search terms and Boolean operators used.

Search	Search terms
#1	Cold AND (weather OR seasonal OR temperature OR “thermal comfort”) OR “indoor temperature”
#2	Indoor OR room OR home OR dwelling OR house OR inside OR housing
#3	“Myocardial infarction” OR coronary OR “heart attack” OR stroke OR angina OR “blood pressure” OR hypothermia OR COPD OR “chronic obstructive pulmonary disease” OR influenza OR flu OR asthma OR bronchitis OR “respiratory disease” OR dementia OR fall OR accident OR injury OR “mental health”“ OR depression OR morbidity OR mortality OR “excess winter deaths”“ OR health OR wellbeing OR physical OR activity
#4	#1 AND #2 AND #3

Data analysis

Included articles were independently assessed by two reviewers (H.J. and B.G.) for quality and risk of bias (good, fair, poor) using the Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies.[18] For each article, data were extracted for country, study design, population, purpose, exposure, outcome(s), results, strengths, and limitations, with data extraction checked (M.R.). Due to heterogeneity in study methodology, population, and outcomes, data were narratively synthesised.

Results

From 1210 references identified through searching, full text copies of 42 studies were obtained and screened, of which 20 studies were included (Fig. 1). Of these, cardiovascular, respiratory, sleep, physical performance and general health outcomes were measured (shown in Table 2). Most studies ($n = 11$) were conducted in older adult populations with varying age ranges (older age was commonly defined in the studies as aged >60 years), eight were in general adults, one in younger adults (23–26 years) and one in children (≤15 years; Table 3). Eleven studies were conducted in Japan,[19–29] four in England,[30–33] and one study each in China,[34] Germany,[35] Taiwan,[36] the United States[37] and Australia.[38] Study quality was rated (see methods) as predominantly fair ($n = 10$) or good ($n = 9$), with only one study rated as poor.[37]

The majority of studies ($n = 18$) recorded temperature inside rooms in participants' homes. Two studies were conducted in laboratory settings under thermal test conditions.[35,36] Most household studies used branded data logger devices to automatically record temperature and humidity ($n = 12$), installed at prescriptive positions (60–110 cm off the floor and away from heat sources). However, the timing of temperature measurement varied across studies (from every 10 min [$n = 10$] to a single time point [$n = 3$]). Most studies ($n = 14$) also collected outdoor temperatures.

Cold temperature thresholds varied across studies, with more than half ($n = 11$) investigating the health effects of a specified indoor temperature at or below 18°C (range 10°C–17.9°C).[19,22,23,26–29,31,34–36,38] In nine studies, analysis drew on a comparison with warmer indoor temperatures.

Cardiovascular health (n = 10)

Half of the included studies (n = 10) explored the impacts of cold indoor temperatures on cardiovascular health, although populations varied across studies (Tables 3 and 4). Four observational studies[20,25,30,31] and two intervention studies[21,24] examined the effects on blood pressure, reporting significant associations between lower indoor temperatures and higher blood pressure. In

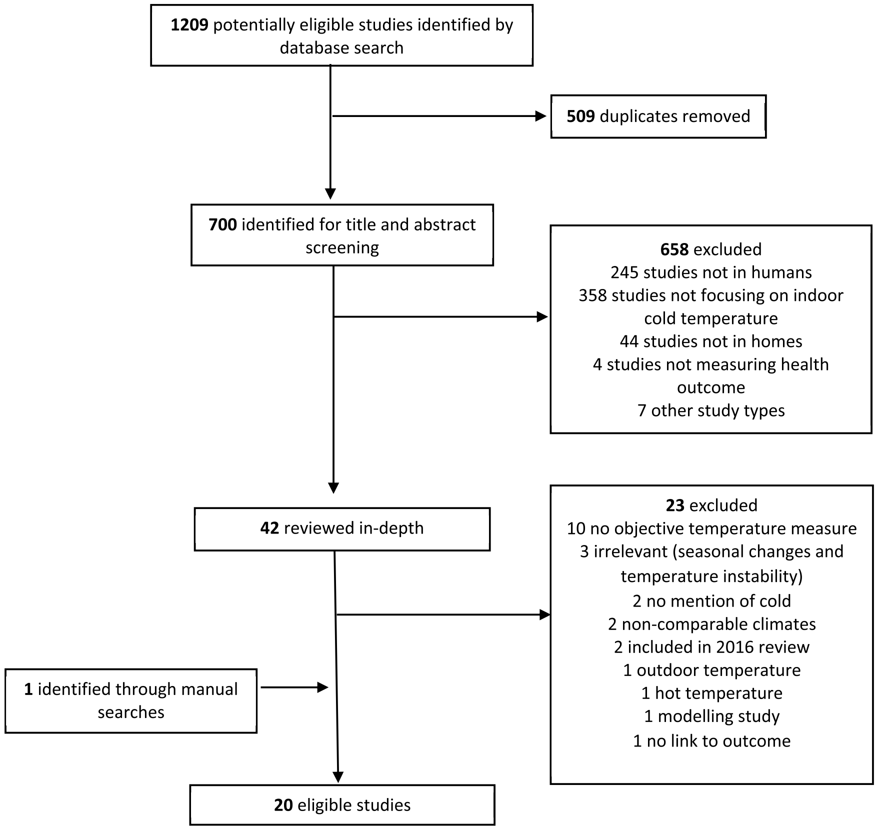

Fig. 1. Study selection flowchart.

Table 2
Outcomes measured in included studies.

Health category	Number of studies	Outcome explored
Cardiovascular	10	Blood pressure,[20,21,24,25,30,31,36] salt intake (linked to blood pressure),[22] electrocardiogram (also known as ECG) abnormalities[29] and blood platelet count[23]
Respiratory	3	Chronic obstructive pulmonary disease symptoms[34] and respiratory viral infection[19,37]
Sleep	2	Nocturia*[27] and sleep onset latency**[26]
Physical performance	2	Physical performance[35] and handgrip strength[28]
General health	3	Perceived impact of cold on health[32] and self-rated health[33,38]

*Needing to wake up more than once at night to urinate. **The time it takes to fall asleep after turning the lights off.

observational studies, changes in blood pressure varied, with increases in systolic blood pressure of 2.2 mm Hg,[20] 4.8 mm Hg,[30] and 8.2 mm Hg[25] recorded per 10°C decrease in temperature. One cross-sectional study explored the differential impacts of cold indoor temperatures by sex and age, finding that older adults and women may be more vulnerable to cold temperature–associated increases in blood pressure than younger adults or men.[25] An experiment investigating overnight temperature exposure under controlled conditions showed that when compared to overnight warmth (24.40 ± 0.78°C), exposure to cold (16.67 ± 0.45°C) increased morning blood pressure in young men with prehypertension.[36]

A cross-sectional study exploring the potential pathways for the effects of cold indoor temperatures on blood pressure found salt intake (measured by nocturnal urinary sodium excretion) was approximately 15% higher in the coldest homes (10.1 ± 2.3°C) compared with the warmest (19.3 ± 1.8°C) and was associated with higher night-time ambulatory blood pressure.[22] Furthermore, two cross-sectional studies showed that cold indoor temperatures <15°C (<14.4°C and <12°C) were associated with higher blood platelet count and increased electrocardiogram abnormalities, which may contribute to increased risk of cardiovascular disease.[23,29]

Respiratory health (n = 3)

Three studies assessed associations between cold indoor temperature and respiratory health (Tables 3 and 4). One prospective cohort study found colder indoor temperatures ≤18.2°C were associated with increased severity of symptoms in patients with COPD.[34] Two studies – one cross-sectional in the general adult population and one prospective cohort of children aged ≤15 years – observed no significant relationship between cold indoor temperatures and symptoms of viral infection.[19,37]

Sleeping problems (n = 2)

One observational study in older adults showed cold indoor temperatures (at 10°C vs 25°C) were associated with greater difficulties initiating sleep, measured by time to sleep or sleep onset

Table 3
Summary of the studies included in the review.

Ref, country, design, QA tool rating	Population	Temperature measurement	Outcome(s) studied
[20]Japan, PC, good	868 home-dwelling men and women (≥60 years)	Living room and bedroom temps (indoor temp) measured day and night 60 cm above the floor. Bed temp at the centre of the bed 50 cm from the headboard. Temps recorded at 10-min intervals using fixed thermo-sensors over 48-h period in winter (Oct-April). Accuracy of indoor temp compared against personal-level environmental temps measured by thermo-sensor attached to ambulatory BP machine.	Daytime SBP, night-time SBP, nocturnal BP fall (%), sleep-trough MBPS (sleep-trough MBPS is the mean SBP in the 120 min after rising minus the lowest night-time BP) and pre-waking MBPS (the difference between mean SBP in the 120 min before and after rising time).
[21]Japan, RCT, good	359 men and women (≥60 years) allocated randomly to either control ($n = 173$) or intervention group ($n = 186$)	Living room temp measured 60 cm above the floor at 10-min intervals using branded data loggers over 48-h period in winter (December to March 2010 and September to March 2011 and 2012).	Indicators of ambulatory BP: sleep-trough MBPS and the pre-waking MBPS. Physical activity. Living room temp.
[22]Japan, P, good	860 home-dwelling men and women (≥60 years)	Living room and bedroom temps (indoor temp) measured 60 cm above the floor. Bed temp at the centre of the bed 50 cm from the headboard. Temps recorded at 10-min intervals using branded data loggers over 48-h period in winter (October to April). The mean ambient temp during the last daytime before the nocturnal urine collection was calculated from indoor temp.	Total nocturnal urinary sodium excretion (mmol) and nocturnal urinary sodium excretion rate (mmol/h). Ambulatory BP. Physical activity.
[23]Japan, CS, good	1095 home-dwelling men and women (≥60 years)	Living room and bedroom temps (indoor temp) measured 60 cm above the floor. Bed temp at the centre of the bed 50 cm from the headboard. Temps recorded at 10-min intervals using branded data loggers over 48-h period in winter (October to April).	After collecting an overnight fasting venous sample with stasis in the morning, PLT counts were measured at a commercial laboratory.
[30]England, CS[a], good	Representative sample of 4659 adults (≥16 years). Pregnant women were excluded.	Living room temp measured once by nurse using a standard digital thermometer, which was kept away from heat sources, such as radiators or sunlight, and hung over the edge of a table where possible (location of measurement and date/time of day not specified).	Mean SBP and DBP measured at 3 × 1-min intervals. The mean of the last two readings was used in the study.
[24]Japan, N-RCT, good	1685 men and women ≥20 years allocated non-randomly either to intervention group (1578 participants) or control group (107 participants).	Living room, bedroom and changing room temps (indoor temp) and relative humidity measured 1.0 m above the floor at 10-min intervals using branded wireless data loggers for 2 weeks over 4 winter periods (November to March).	Change in HBP (follow-up HBP minus HBP measured at baseline).
[29]Japan, CS, good	1480 men and women (≥20 years).	Living room and bedroom temps (indoor temp) and relative humidity measured 1.0 m above the floor at 10-min intervals using branded wireless data loggers for 2 weeks (November to March).	Participants submitted results of a health check-up conducted within a year of the survey, which included the doctor's judgement of whether participants had abnormal ECG waveforms or not.
[31]England, CS,[a] fair	7997 older adults (≥50 years) living in private households, 1301 (16.3%) of whom lived in cold homes.	Indoor temp measured once in the room BP was taken by survey nurse using a digital thermometer, which was placed on a surface away from a radiator and out of direct sunlight. (Location of measurement and date/time of day not specified).	A series of biomarkers that were measured in the blood and lung, including BP and lung function.
[25]Japan, CS, Fair	3514 adults (≥20 years) from 2007 households intending to conduct insulation retrofitting.	Living room, bedroom and changing room temps (indoor temp) and relative humidity measured at 1.0 m above the floor at 10-min intervals using branded wireless data loggers for 2 weeks over 4 winter periods (November to March).	HBP measured twice after 1–2 min resting over period of 2 weeks, at the following times: after getting out of bed in the morning (after urination, before dosing and before breakfast) and before getting into bed in the evening.
[36]Taiwan, CE, fair	24 men (23–26 years): 12 normotensive and 12 prehypertensive.	Room temps controlled by central air conditioning and recorded by a heat-sensitive sensor placed on the forehead and extended into the air. Participants were exposed to two experimental conditions, with at least 1 day in between each exposure.	Comparison of the MBPS after morning awakening under the cold and warm conditions between normotensives and prehypertensives.
[34]China, PC, Fair	82 outpatients with COPD aged 40–85 years.	Bedroom temp and humidity measured using a standard thermo-hygrometer and recorded in diary by participant three times a day (8 am, 2 pm, 8 pm) for 18 months.	Self-reported COPD symptoms were evaluated and categorised by severity from (5) no symptoms to (1) could not tolerate symptoms and had to go to hospital.
[19]Japan, PC, fair	297 children (≤15 years) living in 173 households.	Main types of heating appliances recorded. Night-time bedroom temp measured away from any immediate heating appliances at 15-min intervals using a branded data logger for 3 months (December to February).	Incidence rates of five types of common cold event (catching a cold, having a fever, use of over-the-counter medications for a cold, physician's visit for a cold, absence from school/nursery owing to a cold) and influenza virus infection.
[37]USA, CS, poor	33 households for one winter season (>18 years) living in apartments or condos (mean age 28.5 years).	Indoor temp and relative humidity recorded hourly using 2–4 branded data loggers with at least one in living area and one in bedroom at a height of approximately 1.5 m, away from windows and heating devices and out of direct sunlight for 5–6 months.	Symptoms of respiratory viral infection and sleep quality.
[26]Japan, PC, good	861 home-dwelling men and women (≥60 years).	Living room and bedroom temps (indoor temp) measured 60 cm above the floor. Bed temp at the centre of the bed 50 cm from the headboard. Temps recorded at 10-min intervals using branded data loggers over 48-h period in winter (October to April).	Subjective SOL (sleep diary) and objective SOL (using an actigraph).

Table 3 (*continued*)

Ref, country, design, QA tool rating	Population	Temperature measurement	Outcome(s) studied
[27]Japan, PC, good	1065 home-dwelling men and women (≥60 years).	Living room and bedroom temp (indoor temp) measured 60 cm above the floor. Bed temp at the centre of the bed 50 cm from the headboard. Temps recorded at 10-min intervals using branded data loggers over 48-h period in winter (October to April).	Nocturia, defined as ≥2 nocturnal voids. Nocturnal urine production rate (mL/h) was also calculated.
[35]Germany, CE, fair	88 community-dwelling older women (≥70 years).	Two climate chamber conditions, both assessed in random order with an interval of 1 week. Clothing was standardised. Before and between measurements, the participants were instructed to rest to avoid internal heat production by leg muscle activity.	Primary outcome: muscle power (force × velocity) of lower limbs was assessed using the Nottingham power rig. Secondary outcomes included sit-to-stand performance velocity, walking performance, maximum quadriceps strength and handgrip strength.
[28]Japan, CS, fair	36 home-dwelling older people (mean age 81 years).	Living room, bedroom and dressing room temps measured at 10-min intervals 1.1 m above the floor using branded data loggers for approximately 2 weeks (in December).	Physical performance assessed when people began using rehabilitation facility and repeated every 3 months. Assessed items were grip strength, static postural and balance control assessed by single-leg standing time, and balance and gait function.
[32]England, Q, N/A	Six women and one man (≥66 years).	Living room, bedroom and living room radiator temps measured at 90-min intervals using sensors in 43 participant homes over winter (November to March 2016–2017; location of measurement not specified).	Perceived impact of cold on physical health. Other areas of exploration included whether and how participants achieve suitable internal temps and how they achieve comfort in their homes.
[33]England, CS,[a] fair	74,736 adults (≥16 years) living in England	Indoor temp measured once by survey nurse using a digital thermometer, which was placed on a surface away from a radiator and out of direct sunlight (location of measurement and date/time of day not specified).	Self-rated general health was based on responses to the question, 'How is your health in general?', to provide a binary outcome variable: good health (including very good and good responses) or poor health (including fair, bad and very bad).
[38]South Australia, CS, fair	71 independently living older people (aged 61–98 years) participated in the home monitoring stage of this research.	Main living room air temp, globe temp, relative humidity and air movement measured at 30-min intervals using a data logger placed on a table or sideboard 80–100 cm above the floor, away from any radiation source (e.g. windows), and near where the participant would normally answer the survey. Main bedroom air and globe temps and relative humidity measured using data loggers placed next to the bed, away from any heat source.	Self-rated health and well-being.

BP, blood pressure; COPD, chronic obstructive pulmonary disease; CE, cross-over experimental; CS, cross-sectional; DBP, diastolic blood pressure; ECG, electrocardiogram; HBP, home blood pressure; MBPS, morning blood pressure surge; N-RCT, non-randomised controlled trial; PC, prospective cohort; PLT, blood platelet count; RCT, randomised controlled trial; SBP, systolic blood pressure; SOL, sleep onset latency; Temp, temperature; Q, qualitative.

[a] Secondary analysis using data from the Health Survey for England.

latency.[26] A prospective cohort study found increased nocturia (needing to urinate more than once during the night), an important cause of sleep disturbance in people in colder homes (13.2 ± 3.0°C) compared to those in warmer homes (18.6 ± 2.4°C), particularly among older people (Tables 3 and 4).[27] However, a cross-sectional study of the general adult population found no association between indoor temperatures, which ranged between ~1°C and ~38°C and self-reported sleep problems during the winter season.[37]

Physical performance in older people (n = 2)

Two studies investigated the impact of cold indoor temperatures on the physical performance of older people necessary for independent living (Tables 3 and 4). One experiment found a significant decrease of between 2% and 10% in physical performance in cold indoor temperatures (15°C compared with 25°C), measured by muscle power of lower limbs, an important risk factor for falls and fall injuries in older people.[35] A small cross-sectional study also found older people living in cold homes (<18°C) in winter had poorer handgrip strength compared to those in warm homes (≥18°C).[28]

General self-rated health (n = 3)

The evidence from studies examining the effects of cold indoor temperatures on general health was mixed (Tables 3 and 4). Two studies, one qualitative and the other cross-sectional, found health was perceived to worsen in cold indoor temperatures (<18°C[32] and <~15°C, respectively).[38] In contrast, a large cross-sectional study found people exposed to higher indoor temperatures (each 1°C increase; between temperatures of 7.5°C and 36.8°C) were significantly more likely to report poorer health.[33]

Discussion

The findings of this review update, and are consistent with, those in the 2016 review, which found that cold indoor temperatures were associated with decreased thermal comfort and worse respiratory and cardiovascular health.[3] In the present review, it was shown that cold indoor temperatures in temperate and colder climates may adversely affect a wide range of health outcomes, including cardiovascular (blood pressure, electrocardiogram abnormalities, blood platelet count), respiratory (COPD symptoms, respiratory viral infection), sleep, physical performance and general health. Most reviewed studies (*n* = 17/20) found that cold indoor temperatures were associated with negative effects on health measures.

Overall, considering the evidence from the 2016 review and the findings presented here, the evidence on the risk to cardiovascular health (measured through a range of outcomes) of exposure to cold indoor conditions was consistent. Blood pressure was the most frequently studied outcome measure. A decrease in indoor temperature was shown to be associated with an increase in systolic and diastolic blood pressure[20,25,30,31,36] and higher salt intake,[22] which is independently associated with higher blood pressure, even when confounders, such as physical activity and medical history were considered. The potential health impacts of such blood pressure changes require further study, especially as high blood pressure is the predominant modifiable risk factor for cardiovascular disease, which is currently the leading cause of death

Table 4
Main findings from included studies.

Ref	Purpose	Temp threshold	Results	Limitations
Cardiovascular				
20	To estimate the magnitude of association between indoor temp and ambulatory BP in colder months.	Range was 0.3°C (night) to 33.6°C (morning)	A 1°C decrease in indoor temp was significantly associated with an increase in daytime SBP (0.22 mm Hg; $P = 0.047$), nocturnal % BP fall (0.18%; $P = 0.014$), sleep-trough MBPS (0.33 mm Hg; $P = 0.003$) and pre-waking MBPS (0.31 mm Hg; $P = 0.004$) in adjusted multilevel linear regression models.	Exposure-outcome measured simultaneously so unable to establish causality; non-random sampling means generalisability of study may be limited.
21	To estimate the short-term effectiveness of instruction in home heating on indoor temp and ambulatory BP among elderly people.	Timing intervention with instructions for the heating device to start 1 h before estimated rising time with thermostat set at 24°C.	Indoor temp in the intervention group significantly increased by 2.1°C (14.1°C to 16.2°C) 4 h after rising from bed vs. controls. After adjusting for confounding variables, the increase in temp significantly reduced BP: SBP by −4.43 mm Hg (95% CI −7.88, −0.97) and DBP by −2.33 mm Hg (95% CI −4.58, −0.08).	Assessed short-term effect only; people without heating controller were excluded; consumption of energy (such as electricity or gas) not considered; participants did not achieve the target temp of 24°C so unable to determine the effects of higher indoor temps on BP.
22	To quantify the association between daytime cold exposure in winter and salt intake.	Coldest (10.1 ± 2.3°C) and warmest (19.3 ± 1.8°C) homes.	A comparison of the two groups, adjusting for outdoor temp, showed the nocturnal urinary sodium excretion rate in the coldest homes was 14.2% higher than in the warmest (7.62 vs 6.54 mmol/h respectively). Higher salt intake was also linked to higher night-time ambulatory BP.	Non-random sample; exposure-outcome measured simultaneously, so unable to establish causality; nocturnal urine collection inferior to 24-h collection; lack of information about nutrition, including intake of total energy.
23	To investigate the association between indoor cold exposure and PLT among older people.	Cold (<14.4°C), intermediate (14.4–17.9°C) and warm (>17.9°C).	In the fully adjusted model, PLT count in the cold group was significantly higher compared to intermediate (4.2% lower) and the warm (5.2% lower) groups.	Cannot determine causal directionality from cross-sectional analysis; did not quantify the amount of clothing worn; non-random sampling limits generalisability.
30	To test two hypotheses: (1) a decrease in indoor temp is associated with an increase in BP, independent of other interfering factors; and (2) the indoor temp-BP relationship is moderated by factors, such as mean monthly outdoor temp.	<18°C, ≤18 to <21°C, ≤21 to <24°C and ≥24°C.	After controlling for confounding variables, a 1°C decrease in indoor temp was significantly associated with an increase in BP; 0.48 mm Hg (95% CI −0.72, −0.25) in SBP and 0.45 mm Hg (95% CI −0.63, −0.27) in DBP.	Cross-sectional design and simultaneous measurement of exposure and outcome meant unable to establish causality; single temp measurement; time of measurement not specified.
24	To quantify the changes in HBP due to insulation retrofitting intervention.	Thermal insulation intervention of participants' homes, including heat-insulation work (on the outer walls, floor and/or roof) and replacement of windows and frames.	Morning indoor temp rose by 1.4°C (14.5°C −15.9°C) after insulation retrofitting, despite a 0.2°C decrease in outdoor temp. The intervention significantly reduced morning home SBP by 3.1 mm Hg (95% CI 1.5–4.6) and morning home DBP by 2.1 mm Hg (95% CI 1.1–3.2).	Non-random sample of households that had intention of carrying out insulation retrofitting; differences between intervention and control group at baseline; study could not control the use of heating, accordingly, the frequency of heating may have decreased due to insulation retrofitting.
29	To determine the association between the indoor temp at home and ECG abnormalities.	Cold (<12°C), slightly cold (12°C–18°C) and warm (≥18°C) houses.	Compared to the warm group, the odds ratio of ECG abnormalities in the slightly cold group was 1.79 (95% CI 1.14, 2.81), and in the cold group, it was 2.18 (95% CI 1.27, 3.75).	Potential for selection bias due to health check-up items being omitted at doctor's discretion; unable to test association with specific ECG abnormalities e.g. arrhythmia; standard ECG provides less information than ambulatory ECG.
31	To examine the associations between a cold home (<18°C) and a series of biomarkers measured in the blood and lung.	The analysis compared cold (<18°C) and warm (≥18°C) homes.	SBP and DBP were significantly higher for people living in cold homes compared with people living in warmer homes: SBP was 136.8 vs 133.7 mm Hg, respectively ($P < 0.001$), and DBP was 76.8 vs 74.2 mm Hg, respectively ($P < 0.001$). People in cold homes also had worse handgrip, lower vitamin D levels, higher cholesterol levels, lower white blood cell count, and worse lung conditions.	Cross-sectional design and simultaneous measurement of exposure and outcome meant unable to establish causality; single temp measurement; time of measurement not specified; unadjusted bivariate analysis.
25	To quantify the relationship between HBP and indoor temp.	Mean morning temp was 14.5°C (range 3.3°C–25.2°C), and mean evening temp was 17.8°C (range 4.3°C–27.5°C).	Morning SBP showed significantly higher sensitivity to changes in indoor temp compared with evening SBP (8.2 mm Hg increase/10°C decrease vs 6.5 mm Hg increase/10°C decrease), particularly for older residents and women.	Cannot determine causal directionality from cross-sectional analysis; non-random sample of households that had intention of carrying out insulation retrofitting; no daily survey of clothing.
36	To evaluate the effects of cold exposure during sleep transitions on autonomic functioning and MBPS among young prehypertensives.	24.40 ± 0.78°C (warm condition) or 16.67 ± 0.45°C (cold condition)	Significantly higher MBPS in the period of awakening after sleeping in cold conditions for both prehypertensives and normotensive, but higher trends observed for prehypertensives.	Small, young, male-only sample limits generalisability.
Respiratory				
34	To examine the relationship between indoor/outdoor temp	Average indoor temp ranged between 12.5 ± 2.9°C and	Indoor temp was negatively associated with severe symptoms of COPD (OR 0.95, 95% CI	Exposure-outcome measured simultaneously, so unable to establish

Table 4 (*continued*)

Ref	Purpose	Temp threshold	Results	Limitations
	and humidity on daily self-reported COPD symptoms.	27.1 ± 2.5°C, and humidity from 50.2 ± 11.2% to 72 ± 13.2%, over study period.	0.94, 0.96). The threshold for moving from less to more severe symptoms was 18.2°C. Risk from low indoor temp for COPD patients increased as humidity increased.	causality; indoor temps were recorded by participants and could not be validated; 81% of variations in symptoms were due to baseline health status (influence of environment <19%).
19	To evaluate the relationship between the type of bedroom heater and bedroom temp factors and incidence of common cold among children.	Average time spent <16°C, divided into three groups: <30 min/day (least cold); ≥30 min/day and <180min/day; and ≥180min/day (coldest).	Air conditioners were most prevalent (n = 105, 35%), followed by gas or kerosene heaters (n = 50, 17%), and floor heaters (n = 31, 10%). Air conditioners were associated with higher incidence of all events related to the common cold, especially having a fever (aIRR 1.84, 95% CI 1.41, 2.40). No statistically significant differences in the incidence of common cold in the coldest and least cold night-time temp groups. Children who always felt cold showed a higher incidence of use of over-the-counter medications and physician visits owing to a cold.	Exposure-outcome measured simultaneously, so unable to establish causality; model estimates unadjusted for important confounders, including housing characteristics (e.g. insulation) and socio-economic position; cold symptoms reported by parents could be biased; relatively low response rate (60.7%).
Sleep				
37	To explore the relationship between indoor temp and humidity, perceptions of the indoor environment and self-reported health symptoms.	Temp and humidity perceptions self-reported approximately every 3 weeks. Indoor temp ranged from ~1°C to ~38°C in winter.	No significant association was observed between measured (or perceived) indoor temp or humidity levels in winter and sleep quality or possible or probable viral infection.	Exposure-outcome measured simultaneously, so unable to establish causality; small convenience sample; assumption that perceptions reported 'today' referred to the previous day's temp.
26	To quantify the association between indoor temp in the evening and sleep onset latency (SOL) during the colder seasons in an elderly population.	Mean indoor temp measured in the morning (2 h after getting out of bed), evening (2 h before bedtime) and initial night-time (2 h after bedtime).	A significant inverse association was observed between indoor temp and both subjective and objective measures of SOL. An increase in evening temp from 10°C to 25°C was associated with an estimated decrease in objective SOL from 16.7 min to 12.4 min.	Non-random sampling limits the generalisability of study findings; cannot determine causal directionality from cross-sectional analysis; short study duration (2 nights); short time between exposure (2 h before bedtime) and outcome.
27	To investigate the association between indoor cold exposure and the prevalence of nocturia in an elderly population.	Participants were grouped into warmer (18.6 ± 2.4°C) or colder (13.2 ± 3.0°C) house groups using mean indoor temp measured.	A 1°C decrease in indoor daytime temp was significantly associated with increased likelihood of nocturia, independent of potential confounders and after adjustment for nocturnal urine production rate (OR 1.10, 95% CI 1.04–1.15). Therefore, a 3°C increase in indoor temp from 15.7°C (mean temp among participants with nocturia) to 18.7°C may be associated with a 25% reduction in the prevalence of nocturia.	Non-random sampling limits the generalisability of study findings; cannot determine causal directionality from cross-sectional analysis; voiding frequency only measured over 1 night.
Physical performance				
35	To test the hypothesis that there would be a deterioration in the physical performance of older women during exposure to an indoor cold environment.	Participants were exposed to moderately cold (15°C) and normal/warm (25°C) temp in a climate chamber 45 min before assessment.	There was a statistically significant decrease in physical performance in 15°C room compared with 25°C room, which ranged between 2% and 10%, with only handgrip strength being unaffected by the cold temp.	Non-random sampling of older women limits the external validity of findings.
28	To investigate the effect of seasonal temp differences and cold indoor environments in winter on the physical performance of older people living in the community.	28 participants were classified into the cold group (<18°C) and eight into the warm group (≥18°C).	The results from grip strength and single-leg standing tests showed physical performance was worse in the winter compared to the autumn, and people living in cold houses had worse grip strength in the right hand.	Small, convenience sample prevents findings from being generalised; outcome assessed in rehabilitation facility and not in participants' homes.
General health				
32	To investigate the strategies older people used to stay warm in winter; how these were influenced by attitudes, opinions, and everyday practices; and what prevented the participants from achieving comfort.	7 participants were recruited from 11 homes with median temp <18°C (March 2018).	Most participants felt the cold more than when they were younger. Participants reported a range of chronic health problems, including osteoarthritis and asthma, which appeared to worsen in the cold. Conducting exercise or movement to stay warm was not particularly common.	Small, convenience sample; no objective indicators of health status; qualitative nature means causality cannot be inferred.
33	To investigate the relationship between indoor temp and general health.	Indoor temp ranged from 7.5°C to 36.8°C, with a mean of 20.7°C (standard deviation 2.3).	Each 1°C increase in indoor temp was associated with a 1.7% higher likelihood of poor self-rated health (95% CI 0.7%–2.6%) after adjusting for potential confounders.	Simultaneous measurement of exposure and outcome means no evidence on causal relationship; single temp measurement; time of measurement not specified.
38	To determine links between the indoor thermal environment of housing and self-reported health and well-being in older people.	Average indoor temp ranged from 11°C to 32.7°C over 9-month study period (January to October).	Approximately two-thirds of participants reported 'definitely yes' or 'probably yes' to a negative influence of temp on health and well-being at room temps below about 15°C.	Small, non-random sample limits generalisability of findings; self-reported health effects.

BP, blood pressure; CI, confidence interval; COPD, chronic obstructive pulmonary disease; DBP, diastolic blood pressure; ECG, electrocardiogram; HBP, home blood pressure; MBPS, morning blood pressure surge; OR, odds ratio; PLT, blood platelet count; SBP, systolic blood pressure; SOL, sleep onset latency; Temp, temperature.

globally.[39–41] Higher blood pressure sensitivity to cold indoor temperatures in older adults and women could be due to less muscle mass and subsequently less metabolic heat production.[25] Older adults are particularly susceptible to developing cardiovascular disease[42] and are less likely to feel the cold and may not adapt their behaviour accordingly, such as adding layers of clothes.[25] Two studies, rated here as good quality, suggested that interventions that increase indoor temperatures can lower blood pressure,[21,24] although the duration of these effects is unknown. These findings are consistent with a study that found lower blood pressure among a homogenous population living in blocks of flats following energy efficiency housing improvements.[43] This review also identified the impacts of cold indoor temperatures on non-blood pressure risk factors and biomarkers of cardiovascular disease, including increased electrocardiogram abnormalities[29] and higher blood platelet count,[23] both shown to increase the risk of cardiovascular disease in other population-based cohort studies.[44–47]

Findings reported in the reviewed studies suggest that night-time bedroom temperatures <18°C (10°C and 13.2 ± 3.0°C, respectively) can increase sleep problems,[26] as well as the incidence of conditions such as nocturia-associated sleep disturbance in older adults.[27] Sleep is a well-known determinant of health, well-being and quality of life, and insufficient or poor quality sleep has been linked to type 2 diabetes, cardiovascular disease, obesity, and depression.[48–50] The prevalence of sleep-disturbing problems such as nocturia increase with age and may reflect comorbid physical and mental health conditions,[51] an area that needs further exploration in the context of cold indoor temperatures.

The findings in the current review indicate that physical performance, a known determinant of quality of life particularly for older people,[52] can decrease following exposure to cold indoor temperatures.[28,35] Prolonged exposure to cold temperatures may decrease grip strength, which for older frail people can increase the risk of future cognitive deterioration, disability, hospitalisation and all-cause mortality.[53,54] However, both studies identified in this review measured physical performance outside of the home (in a laboratory and rehabilitation centre). Future studies should therefore measure these effects within the home to accurately reflect personal exposure to cold indoor temperatures.

Evidence on the effects of cold indoor temperatures on respiratory and general self-rated health outcomes was mixed. Adults with COPD reported worsening symptoms when exposed to colder indoor temperatures ≤18.2°C.[34] This is consistent with evidence from a previous review, which identified better respiratory symptom scores among older adults (aged ≥65 years) with COPD who spent more days with living room temperatures ≥21°C (+9 hours).[3] For healthy adult and child populations, studies found no significant relationship between cold indoor temperatures and symptoms of viral infection.[19,37] This evidence was rated as fair and poor, respectively, suggesting the merit of further research in this area. Two studies connected cold indoor temperatures with the perception of deteriorating health.[32,38] In contrast, another study observed a small but significant association between each 1°C increase in indoor temperature (between temperatures of 7.5°C and 36.8°C) and poor self-rated health.[33] However, people with worse self-rated health may maintain higher indoor temperatures for personal preference or following advice from professionals. Difference in tenure type (such as social housing compared to privately rented) may also impact temperatures achieved.[33]

Several gaps in the evidence have been identified from this review. A predominant focus of many studies has been on the impacts of cold indoor temperatures in older adult populations due to their increased vulnerability to cold temperatures and because certain cold-related conditions (e.g. nocturia) are more apparent in this population. Nevertheless, no evidence was identified on the relationship between cold indoor temperatures and frailty (e.g. Alzheimer's, falls, hospital admissions, time spent in recovery), the duration of exposure that leads to illness, or the long-term health and well-being effects of exposure to low indoor temperatures. More research is needed to understand the impact of cold indoor temperatures on people with different chronic health conditions due to a limited number of studies in this area.[55–57] Further research should also investigate the impact of cold indoor temperature among children,[19,58] particularly respiratory disease, which accounts for most of the excess winter health burden in children.[14]

To date, no studies have explored the mental health and well-being impacts of objectively measured cold indoor temperatures in the home. Previous research using a subjective measure has shown that a lack of thermal comfort at home increases the likelihood of severe mental distress[59] and that energy efficiency improvements have a positive effect on psychological, social, and financial well-being.[60–62] This review also identified no studies using objectively measured temperature to explore health outcomes in terms of wider contextual factors such as fuel poverty or poor quality housing (e.g. dwellings in the United Kingdom that contain a Category 1 Hazard under the Housing Health and Safety Rating System),[63] which may exacerbate the effects of cold indoor temperature on health and well-being. Nevertheless, a longitudinal study using a subjective measure of energy poverty investigated the effect on mental health, cardiovascular disease and respiratory health.[64] This study found that when people could not afford to heat their homes (i.e. energy poverty), their mental health worsened, and the odds of reporting depression/anxiety or hypertension increased.[64] Furthermore, the interrelationship between indoor temperature, humidity (possibly leading to condensation and associated mould) and air quality (including ventilation)[6] may alter the impact of cold indoor temperatures on health.

More than half of the studies included in this review found cold indoor temperatures <18°C − the minimum recommended home temperature threshold[3,14] − were associated with negative effects on health.[19,22,23,26–29,31,34–36,38] In addition, some studies linked better health outcomes with indoor temperatures >23°C when compared to temperatures <18°C.[26,35,36] Only one study found that increased indoor temperature was linked to the likelihood of a poor outcome (poor self-rated health).[33] A single randomised controlled trial found that instructions for older adults to heat their living room to 24°C 1 h before rising out of bed increased average temperatures by 2.1°C (14.1°C–16.2°C) and significantly reduced blood pressure 4 hours after rising.[21] Such findings suggest that setting indoor temperature threshold guidance may help to improve health in target populations. Alternative interventions that improve indoor temperatures, such as insulation retrofitting of homes, have shown similar improvements to morning blood pressure,[24] which may be worthy of future research. Further understanding of energy prices is warranted to explore any associations with temperatures in home settings and health and well-being outcomes and to assist in the identification of vulnerable populations.

Public health advice on minimum home temperatures may help to mitigate serious health risks associated with cold indoor temperatures, especially in vulnerable populations, such as older adults. Generally, indoor temperatures of <18°C are associated with negative health effects. However, the evidence summarised in this review is not sufficient or strong enough to draw firm conclusions on the specific temperature thresholds at which health effects begin for different population groups.

Limitations

There are several limitations to this review, which should be considered when interpreting the findings. Due to time constraints, searches were limited to seven databases. However, a good variety of databases were used, the search adopted a systematic approach, and the inclusion criteria were widened compared to the 2016 review to include social outcomes, studies using secondary data and intervention studies. Two reviewers independently decided on study inclusion with conflict resolution, minimising the risk of bias and error. The review was limited to studies conducted in temperate and colder climates due to the increased risk of morbidity and mortality during winter,[65] so wider evidence from other countries has been excluded. Restricting the studies to English language only may have also led to the exclusion of relevant studies. All included studies were required to record temperatures using an objective measure, limiting the bias of perceived temperatures. Thus, studies that did not record objective temperature measurements were excluded, which may have led to the exclusion of studies exploring relevant outcomes, for example, the longitudinal study on energy poverty and health outcomes described earlier.[64] Limitations across included studies are presented in Table 4.

Conclusion

The findings from this review identify that cold indoor temperatures can negatively impact a wide range of health measures, including those related to cardiovascular and respiratory health, sleep, physical performance and general health. This evidence is consistent with, and builds on, findings in the 2016 systematic literature review on the topic.[3] Some health risks gradually increased as temperatures decreased <18°C but varied according to chronic health condition and age. Nevertheless, limitations within studies and study heterogeneity make it difficult to establish if temperatures slightly below or above 18°C may also be safe for health. Further research into the specific temperature thresholds for overall health and well-being in a range of populations is needed to inform future temperature recommendations.

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Competing interests

None declared.

References

1. Azam S, Jones T, Wood S, Bebbington E, Woodfine L, Bellis M. *Improving winter health and well-being and reducing winter pressures in Wales. A preventative approach*. Cardiff: Public Health Wales; 2019.
2. Liddell C, Guiney C. Living in a cold and damp home: frameworks for understanding impacts on mental well-being. *Publ Health* 2015;**129**(3):191–9.
3. Jevons R, Carmichael C, Crossley A, Bone A. Minimum indoor temperature threshold recommendations for English homes in winter – a systematic review. *Publ Health [Internet]* 2016;**136**:4–12. https://pubmed.ncbi.nlm.nih.gov/27106281/.
4. Braubach M, Jacobs DE, Ormandy D. *Environmental burden of disease associated with inadequate housing: a method guide to the quantification of health effects of selected housing risks in the WHO European Region*. Copenhagen: WHO Regional Office for Europe; 2011.
5. Thomson H, Thomas S, Sellstrom E, Petticrew M. Housing improvements for health and associated socioeconomic outcomes (Review). *Cochrane Database Syst Rev* 2013;(2):1–372.
6. World Health Organization. *WHO Housing and health guidelines [Internet]*. 2018. Geneva; Available from: https://www.who.int/publications/i/item/9789241550376.
7. Wang Q, Li C, Guo Y, Barnett AG, Tong S, Phung D, et al. Environmental ambient temperature and blood pressure in adults: a systematic review and meta-analysis. *Sci Total Environ* 2017;**575**:276–86.
8. Cotter N, Monahan E, McAvoy H, Goodman P. Coping with the cold - exploring relationships between cold housing, health and social wellbeing in a sample of older people in Ireland. *Qual Ageing* 2012;**13**(1):38–47.
9. Hills J. *Getting the measure of fuel poverty: final report of the fuel poverty review*, vol. 72. London: CASE report; 2012.
10. Department of Health. *Cold Weather Plan for England: protecting health and reducing harm from severe cold*. London: Best Practice Guidance; 2011.
11. UK Health Security Agency. *The Cold Weather Plan for England Protecting health and reducing harm from cold weather [Internet]*. London: Department of Health Guidance; 2021 [cited 2023 Jun 15]. Available from: https://webarchive.nationalarchives.gov.uk/ukgwa/20230418173952/. https://www.gov.uk/government/publications/cold-weather-plan-cwp-for-england.
12. World Health Organization. *Regional Office for Europe. Health impact of low indoor temperatures. Copenhagen*. 1987.
13. World Health Organization. *Regional office for Europe. Housing, energy and thermal comfort. Copenhagen*. 2007.
14. World Health Organization. *WHO Housing and health guidelines. Geneva*. 2018.
15. Broadbent P, Thomson R, Kopasker D, McCartney G, Meier P, Richiardi M, et al. The public health implications of the cost-of-living crisis: outlining mechanisms and modelling consequences. *The Lancet Regional Health - Europe* 2023;**27**:100585.
16. The Lancet Regional Health – Europe. The cost-of-living crisis is also a health crisis. *The Lancet Regional Health - Europe* 2023;**27**:100632.
17. Middlemiss L, Ambrose A, Simcock N, Martiskainen M, Sherif G. Fuel poverty in the cost of living crisis. *Leeds* 2022.
18. National Heart, Lung and Blood Institute. *Study quality assessment tools [Internet]*. 2021 [cited 2021 Nov 2]. Available from: https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools.
19. Ishimaru T, Mine Y, Odgerel CO, Miyake F, Kubo T, Ikaga T, et al. Prospective cohort study of bedroom heating and risk of common cold in children. *Pediatr Int* 2022;**64**(1):e14755.
20. Saeki K, Obayashi K, Iwamoto J, Tone N, Okamoto N, Tomioka K, et al. Stronger association of indoor temperature than outdoor temperature with blood pressure in colder months. *J Hypertens* 2014;**32**(8):1582–9.
21. Saeki K, Obayashi K, Kurumatani N. Short-term effects of instruction in home heating on indoor temperature and blood pressure in elderly people: a randomized controlled trial. *J Hypertens* 2015;**33**(11):2338–43.
22. Saeki K, Obayashi K, Tone N, Kurumatani N. Daytime cold exposure and salt intake based on nocturnal urinary sodium excretion: a cross-sectional analysis of the HEIJO-KYO study. *Physiol Behav* 2015;**152**:300–6.
23. Saeki K, Obayashi K, Kurumatani N. Platelet count and indoor cold exposure among elderly people: a cross-sectional analysis of the HEIJO-KYO study. *J Epidemiol* 2017;**27**(12):562–7.
24. Umishio W, Ikaga T, Kario K, Fujino Y, Hoshi T, Ando S, et al. Intervention study of the effect of insulation retrofitting on home blood pressure in winter: a nationwide Smart Wellness Housing survey. *J Hypertens* 2020;**38**(12):2510–8.
25. Umishio W, Ikaga T, Kario K, Fujino Y, Hoshi T, Ando S, et al. Cross-sectional analysis of the relationship between home blood pressure and indoor temperature in winter: a nationwide smart wellness housing survey in Japan. *Hypertension* 2019;**74**(4):756–66.
26. Saeki K, Obayashi K, Tone N, Kurumatani N. A warmer indoor environment in the evening and shorter sleep onset latency in winter: the HEIJO-KYO study. *Physiol Behav* 2015;**149**:29–34.
27. Saeki K, Obayashi K, Kurumatani N. Indoor cold exposure and nocturia: a cross-sectional analysis of the HEIJO-KYO study. *BJU Int* 2016;**117**(5):829–35.
28. Hayashi Y, Schmidt SM, Fänge AM, Hoshi T, Ikaga T. Lower physical performance in colder seasons and colder houses: evidence from a field study on older people living in the community. *Int J Environ Res Publ Health* 2017;**14**(651).
29. Umishio W, Ikaga T, Kario K, Fujino Y, Suzuki M, Ando S, et al. Electrocardiogram abnormalities in residents in cold homes: a cross-sectional analysis of the nationwide Smart Wellness Housing survey in Japan. *Environ Health Prev Med* 2021;**26**(104).
30. Zhao H, Jivraj S, Moody A. "My blood pressure is low today, do you have the heating on?" The association between indoor temperature and blood pressure. *J Hypertens* 2019;**37**(3):504–12.
31. Shiue I. Cold homes are associated with poor biomarkers and less blood pressure check-up: English Longitudinal Study of Ageing, 2012–2013. *Environ Sci Pollut Control Ser* 2016;**23**(7):7055–9.
32. Hughes C, Natarajan S. 'The older I get, the colder I get'—older people's perspectives on coping in cold homes. *J Hous Elder* 2019;**33**(4):337–57.
33. Sutton-Klein J, Moody A, Hamilton I, Mindell JS. Associations between indoor temperature, self-rated health and socioeconomic position in a cross-sectional study of adults in England. *BMJ Open* 2021;**11**(2):1–11.

34. Mu Z, Chen PL, Geng FH, Ren L, Gu WC, Ma JY, et al. Synergistic effects of temperature and humidity on the symptoms of COPD patients. *Int J Biometeorol* 2017;**61**(11):1919–25.
35. Lindemann U, Oksa J, Skelton DA, Beyer N, Klenk J, Zscheile J, et al. Effect of cold indoor environment on physical performance of older women living in the community. *Age Ageing* 2014;**43**(4):571–5.
36. Hong CH, Kuo TBJ, Huang BC, Lin YC, Kuo KL, Chern CM, et al. Cold exposure can induce an exaggerated early-morning blood pressure surge in young prehypertensives. *PLoS One* 2016;**11**(2):e0150136.
37. Quinn A, Shaman J. Health symptoms in relation to temperature, humidity, and self-reported perceptions of climate in New York City residential environments. *Int J Biometeorol* 2017;**61**(7):1209–20.
38. Hansen A, Williamson T, Pisaniello D, Bennetts H, van Hoof J, Martins LA, et al. The thermal environment of housing and its implications for the health of older people in south Australia: a mixed-methods study. *Atmosphere* 2022;**13**(1).
39. Bhatnagar P, Wickramasinghe K, Wilkins E, Townsend N. Trends in the epidemiology of cardiovascular disease in the UK. *Heart* 2016;**102**(24):1945–52.
40. Fuchs FD, Whelton PK. High blood pressure and cardiovascular disease. *Hypertension* 2020;**75**(2):285–92.
41. World Health Organization. *Cardiovascular diseases (CVDs) [Internet]*. 2021 [cited 2023 Jan 3]. Available from: https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds.
42. Rodgers JL, Jones J, Bolleddu SI, Vanthenapalli S, Rodgers LE, Shah K, et al. Cardiovascular risks associated with gender and aging. *J Cardiovasc Dev Dis* 2019;**6**(2).
43. Lloyd EL, McCormack C, McKeever M, Syme M. The effect of improving the thermal quality of cold housing on blood pressure and general health: a research note. *J Epidemiol Community Health* 2008;**62**(9):793–7.
44. Sloan A, Gona P, Johnson AD. Cardiovascular correlates of platelet count and volume in the Framingham Heart Study. *Ann Epidemiol* 2015;**25**(7):492–8.
45. Vinholt PJ, Hvas AM, Frederiksen H, Bathum L, Jørgensen MK, Nybo M. Platelet count is associated with cardiovascular disease, cancer and mortality: a population-based cohort study. *Thromb Res* 2016;**148**:136–42.
46. Auer R, Bauer DC, Marques-Vidal P, Butler J, Min LJ, Cornuz J, et al. Association of major and minor ECG abnormalities with coronary heart disease events. *JAMA* 2012;**307**(14):1497–505.
47. Groot A, Bots ML, Rutten FH, den Ruijter HM, Numans ME, Vaartjes I. Measurement of ECG abnormalities and cardiovascular risk classification: a cohort study of primary care patients in The Netherlands. *Br J Gen Pract* 2015;**65**(630):e1–8.
48. Ferrie JE, Kumari M, Salo P, Singh-Manoux A, Kivimäki M. Sleep epidemiology—a rapidly growing field. *Int J Epidemiol* 2011;**40**(6):1431–7.
49. Bertisch SM, Pollock BD, Mittleman MA, Buysse DJ, Bazzano LA, Gottlieb DJ, et al. Insomnia with objective short sleep duration and risk of incident cardiovascular disease and all-cause mortality: sleep Heart Health Study. *Sleep* 2018;**41**(6).
50. Centers for Disease Control and Prevention. *Sleep and sleep disorders [Internet]*. 2020 [cited 2022 Aug 3]. Available from: https://www.cdc.gov/sleep/index.html.
51. Bliwise DL, Wagg A, Sand PK. Nocturia: a highly prevalent disorder with multifaceted consequences. *Urology* 2019;**133S**:3–13.
52. Fusco O, Ferrini A, Santoro M, Lo Monaco MR, Gambassi G, Cesari M. Physical function and perceived quality of life in older persons. *Aging Clin Exp Res* 2012;**24**(1):68–73.
53. Ling CHY, Taekema D, de Craen AJM, Gussekloo J, Westendorp RGJ, Maier AB. Handgrip strength and mortality in the oldest old population: the Leiden 85-plus study. *Can Med Assoc J* 2010;**182**(5):429–35.
54. Bohannon RW. Hand-grip dynamometry predicts future outcomes in aging adults. *J Geriatr Phys Ther* 2008;**31**(1).
55. Osman LM, Ayres JG, Garden C, Reglitz K, Lyon J, Douglas JG. Home warmth and health status of COPD patients. *Eur J Publ Health [Internet]* 2008;**18**(4):399–405 [cited 2023 Apr 19], https://academic.oup.com/eurpub/article/18/4/399/476619.
56. Hong CH, Kuo TBJ, Huang BC, Lin YC, Kuo KL, Chern CM, et al. Cold exposure can induce an exaggerated early-morning blood pressure surge in young prehypertensives. *PLoS One [Internet]* 2016;**11**(2):e0150136 [cited 2023 Apr 19], https://pubmed.ncbi.nlm.nih.gov/26919177/.
57. Mu Z, Chen PL, Geng FH, Ren L, Gu WC, Ma JY, et al. Synergistic effects of temperature and humidity on the symptoms of COPD patients. *Int J Biometeorol [Internet]* 2017;**61**(11):1919–25 [cited 2023 Apr 19], https://pubmed.ncbi.nlm.nih.gov/28567499/.
58. Ross A, Collins M, Sanders C. Upper respiratory tract infection in children, domestic temperatures, and humidity. *J Epidemiol Community Health* 1990;**44**(2):142–6.
59. Clair A, Baker E. Cold homes and mental health harm: evidence from the UK household longitudinal study. *Soc Sci Med [Internet]* 2022;**314**:115461. https://www.sciencedirect.com/science/article/pii/S0277953622007675.
60. Green G, Gilbertson J. *Warm front better health: health impact evaluation of the warm front scheme*. Sheffield: Centre for Regional, Economic and Social Research; 2008.
61. Grey CNB, Schmieder-Gaite T, Jiang S, Nascimento C, Poortinga W. Cold homes, fuel poverty and energy efficiency improvements: a longitudinal focus group approach. *Indoor Built Environ* 2017;**26**(7):902–13.
62. Liddell C. *Estimating the health impacts of Northern Ireland's warm homes scheme 2000-2008*. 2008.
63. Office of the Deputy Prime Minister. *Housing health and safety: rating system: operating guidance: housing Act 2004 Guidance about inspections and assessment of hazards given under Section 9*. 2006. London.
64. Bentley R, Daniel L, Li Y, Baker E, Li A. The effect of energy poverty on mental health, cardiovascular disease and respiratory health: a longitudinal analysis. *The Lancet Regional Health - Western Pacific* 2023;**35**:1–13.
65. Healy JD. Excess winter mortality in Europe: a cross country analysis identifying key risk factors. *J Epidemiol Community Health* 2003;**57**(10):784–9.

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Letter to the Editor

Community-based sharing of vaccine adverse event information for public trust: a case of Soma city in Fukushima, Japan

A lesson learned from the COVID-19 pandemic is the importance of having a robust public health infrastructure that can facilitate swift and effective responses to future pandemics.[1] Vaccine hesitancy and antivaccine activism, however, persist as major obstacles to attaining comprehensive vaccine coverage across populations.[2] Public trust in the government is crucial in determining vaccine uptake.[3] The 2011 Fukushima disaster in Japan resulted in the worst consequence: a nuclear powerplant accident from a catastrophic 9.0 magnitude earthquake and subsequent tsunami. Despite this, the local government and the community successfully established disaster relief efforts. This letter highlights the efforts in promoting the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccinations in Soma (Fukushima, Japan), a city near the epicenter of the 2011 East Japan Earthquake and the subsequent nuclear power plant disaster, while concurrently sharing adverse event (AE) information with the community.

The city initiated the mass SARS-CoV-2 vaccination in May 2021 (Supplemental Figure S1). The community-based mass vaccination was implemented, applying the experience of disaster relief efforts (Supplemental Methods and Supplemental Figure S2). The city surveyed AEs after vaccination in the residents and kept them informed of their findings on the Web site. The severity of AEs was reported as either '*mild*' (AEs not interfering with daily life and work) or '*moderate to severe*' (AEs causing disruptions to daily life and work) to simplify the response process for participants.

The vaccine coverage of the initial two doses and the third and fourth doses for the population aged ≥65 years were 94.2%, 92.0%, and 84.4%, respectively, as of September 25, 2022. A recent safety report, including city officers and healthcare professionals, supports feasible safety profiles of booster administration (Supplemental Table S1 and Fig. 1). No elevation in the proportions of individuals with AEs was seen after the third and fourth doses of booster administration. Similar safety profiles were observed between two different messenger RNA vaccines for the first and the second booster (Supplemental Figure S3). Safety profiles in the adolescent population were also shared with Soma citizens (Supplemental Figure S4 and Supplemental Table S2). The limitation, however, includes a small cohort, which might not capture uncommon AEs, potential overestimation of AEs because of a recipient-oriented survey, lack of standardization in assessing AE severity, and no inclusion of older people who retired from the city office or medical institutions.

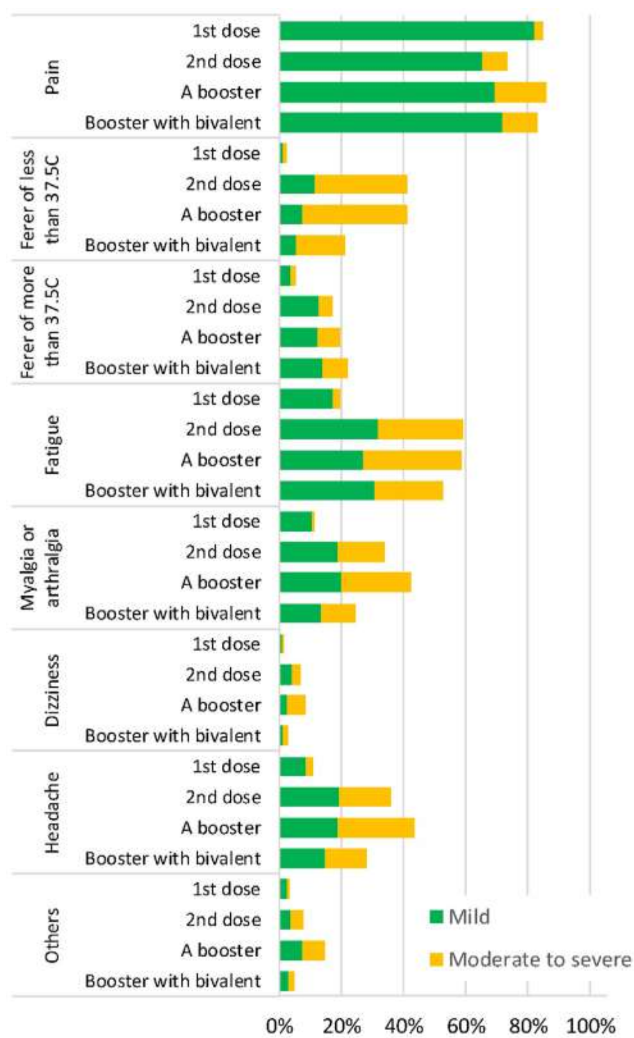

Fig. 1. Results of the safety survey for the SARS-CoV-2 vaccination.
The results of the questionnaire survey on AEs after the SARS-CoV-2 vaccination are shown. The percentages of AEs are shown by dose ($n = 488$, 474, 459, and 375 for first, second, first booster, and second booster administrations, respectively) and by severity. The severity was answered by 'mild' (AEs without interference with daily life and work) or 'moderate to severe' (AEs causing interference with daily life and work).

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Vaccination is a priority issue for disaster relief efforts, as Türkiye's physician's correspondence in the recent *Lancet*.[4] Publicizing vaccine safety information might potentially hinder the efforts to promote vaccination due to causing the fear of AEs in the citizen. Despite this concern, Soma city conducted a safety survey among residents and achieved high vaccine coverage. A randomized study in the United States was reported to investigate whether the disclosure of AE information enhanced the trust in the Centers for Disease Control and Prevention and improved perceptions of vaccine benefits.[5] The study found that the highest levels of trust and vaccine acceptance were observed in the group provided with both the vaccine information statement and the AE summary. The study also indicated that the exposure to individual reports on the serious AEs, such as cases of deaths or permanent disabilities, could potentially diminish both trust and acceptance. Thus, providing transparent and balanced vaccine information is crucial in fostering public trust in immunization programs. In the case of Soma, the health officials shared the descriptive statistics as shown in Figure, not individual AEs, which might also help preventing vaccine hesitancy in the community. Sharing the safety issues on a community level would support the comprehensive and efficient rollout of vaccinations in the future pandemic.

Author statements

Ethical approval

None sought.

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Competing interests

The authors declare no conflict of interest in this article.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.puhe.2023.05.015.

References

1. The Lancet. Moving past the COVID-19 emergency in the USA. *Lancet* 2023;**401**(10386):1399.
2. Carpiano RM, Callaghan T, DiResta R, Brewer NT, Clinton C, Galvani AP, et al. Confronting the evolution and expansion of anti-vaccine activism in the USA in the COVID-19 era. *Lancet* 2023;**401**(10380):967–70.
3. Miyachi T, Takita M, Senoo Y, Yamamoto K. Lower trust in national government links to no history of vaccination. *Lancet* 2020;**395**(10217):31–2.
4. Alomari O. Why vaccinations should be a top priority in earthquake relief efforts. *Lancet* 2023;**401**(10384):1263–4.
5. Scherer LD, Shaffer VA, Patel N, Zikmund-Fisher BJ. Can the vaccine adverse event reporting system be used to increase vaccine acceptance and trust? *Vaccine* 2016;**34**(21):2424–9.

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Original Research

COVID-19 associated with universities in England, October 2020–February 2022

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ABSTRACT

Objectives: The aim of this study was to describe the epidemiology of COVID-19 cases at universities in England (October 2020–February 2022) and investigate factors associated with rates of COVID-19 among students during autumn/winter of 2021/22.
Study design: The study was an observational retrospective study using routine contact tracing data.
Methods: Estimates of COVID-19 cases among students and staff at universities were described. Student cases aged 18–24 years were calculated as a percentage of all cases within that age group. Count regression was used to explore university characteristics associated with case numbers.
Results: We identified 102,382 cases among students and 28,639 among staff. Student cases reflected trends in the wider population of the same age group, but the observed fraction aged 18–24 years who were students was consistently below the expected level (32%). Phased reopening of universities in March–May 2021 was associated with small peaks but low absolute numbers. Russell group membership, campus universities, and higher student proportions in halls of residence were all associated with increased case numbers.
Conclusions: COVID-19 case numbers among students in England varied considerably. At no time were the observed case numbers as high as expected from community prevalence. Characteristics of universities associated with higher case rates can inform future guidance for higher education settings.

Introduction

During the COVID-19 pandemic in the United Kingdom (UK), universities and higher education settings were recognised as settings which could support sustained transmission. Early mathematical-modelling studies concluded that without interventions, there was a risk of very high case numbers.[1,2] Later models estimated that even with full adherence to isolation rules, prevalence could reach 22% (approximately 500,000 students) in Autumn 2021.[1] Student adherence is a key parameter for predictive modelling, with estimated prevalence varying from 4% to 21% depending on the strength of social distancing and mask wearing.[3] While analysis suggested that densely populated halls of residence may be associated with high rates of transmission,[4] media interest was also focussed on cross-country migration[5] and social gatherings.[6] Policy and guidelines on COVID-19 prevention in higher education settings in the UK were supplemented by university-led interventions.

Following the start of the autumn 2020 term (approximately September–December), student case rates in English university towns doubled and were largely driven by residential outbreaks in student accommodation.[7] This was despite campuses reopening with safety measures in September 2020 following the end of first national lockdown in England.[8] Phylogenetic studies at the Universities of Cambridge[9] and Glasgow[10] showed evidence of transmission through student accommodation in autumn 2020, with rates declining following the introduction of household isolation and the offer of individual screening. Minimal evidence of crossover between students and staff, or students and the wider community was found, in contrast to a previous finding of spillover from students to the wider population of 18–23-year-olds in England.[7] Further prevention measures at universities included closures between 3 December 2020 and 8 March 2021[11,12] (coinciding with the

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third national lockdown 5 January–8 March 2021), followed by a phased reopening in spring 2021, following the third national lockdown.[12]

Interventions and safety measures to reduce transmission of COVID-19 at universities were not without cost; studies have shown post-traumatic stress disorder,[13] general anxiety disorder,[14] and clinical depression[15–17] to all be associated with these restrictions. Longitudinal studies show that students also experienced worse sleep quality,[18] insomnia symptoms,[19] lower physical activity,[20] and smartphone addiction[15] during lockdowns. There were also challenges for universities not only in implementing safety measures but also in maintaining academic standards[21] and dealing with the reduced income from fewer international students.[22]

There have been no studies to report cases of COVID-19 associated with universities in England on a national scale and to consider how case numbers varied between different institutions. Universities are varied in the range of courses offered, physical layout (such as whether they are a campus-focused university), accommodation settings used by students and the make-up of the student body (such as number of postgraduate and international students). These factors may have modified the risk of COVID-19 transmission during the course of the pandemic, and understanding the nature of this variation can help inform future guidance and policy to prevent respiratory virus infection at these settings.

Using routinely collected contact tracing data in England, this study first describes cases of COVID-19 among students and staff at higher education settings during 18 months of the first two years of the pandemic (October 2020–February 2022). Secondly, we used available data on university makeup and characteristics to investigate factors associated with rates of COVID-19 among students at universities during autumn/winter of 2021/22.

Methods

Data sources

Contact tracing data

Contact tracing data were obtained from the routine, national contact tracing system in England (NHS Test and Trace), where cases were defined as people testing positive for SARS-CoV-2 by PCR and referred for contact tracing.

As part of contact tracing, individuals were asked to list activities undertaken in the 7 days prior to onset of symptoms (or positive test for asymptomatic cases), including location category, date of attendance, address, and postcode. Cases were included if they completed contact tracing between 23 October 2020 (start of collection of detailed setting data, including education) and 23 February 2022 (end of routine contact tracing). Individuals who were referred to contact tracing on multiple occasions (as a result of re-infection) were recorded as multiple cases within the dataset.

Population and university data

The Office for National Statistics (ONS) mid-2020 dataset was used to obtain population estimates for the number of 18–24-year-olds in England (available from: https://www.ons.gov.uk). Numbers of registered students for the 2020/21 academic year (all enrolments), student breakdown (numbers of undergraduate students, numbers of international students), domicile location of students (unitary local authority of permanent home address prior to university entry), numbers of students in halls of residence (provider- and privately-owned), and courses offered (medicine and dentistry, creative arts, engineering and technology) were obtained from the Higher Education Statistics Agency (HESA; available from: https://www.hesa.ac.uk/data-and-analysis/students). Publicly available sources were used for a list of campus-based universities[23] and Russell group members (24 leading UK universities with a focus on research and reputation for high academic achievement).[24]

Definition of university-associated cases

Cases were defined as university students if they reported an activity of "attending childcare, school, educational setting" and selected "university" for the setting of this activity. Cases were defined as university staff if they reported an activity of "teaching and education" and setting of "university" and were aged ≥18 years. Where individuals reported multiple activities at a university during a contact tracing episode, the first activity was used for analysis. As vaccination strategies and other policy interventions will have impacted case rates for different age groups over time, analysis of student cases was restricted to those aged 18–24 years-old.

Matching cases to specific universities

A list of universities was produced by combining and deduplicating the Office for Students register[25] and a list of higher education providers supplied by the Department for Education. Universities were excluded from the analysis if they were outside of England, had multiple study sites across different towns or cities, did not award degrees, were no longer offering courses in April 2022, did not have their own classrooms (such as satellite institutes whose degrees were awarded by other institutions or utilised facilities of another institution), were predominantly distance-learning based, or did not offer undergraduate courses.

Student and staff cases were matched to a specific university using the location name, address, and postcode of the setting provided during contact tracing. A set of keywords was generated for each university in an iterative process to maximise matching accuracy. Matching was undertaken using the "fuzzyjoin" package in R to allow for variations and typographic errors in how the names of specific institutions had been recorded. Matching accuracy was tested by manually checking five sets of 1000 randomly sampled cases.

Data analysis

All data manipulation and analysis were undertaken using R version 4.0.3.[26]

Descriptive epidemiology

Cases were aggregated by week of the first reported university activity between October 2020 and February 2022. Case numbers were described over time and as a percentage of the total number of cases reported to the contact tracing system (18–24 years for student cases, ≥18 years for staff cases).

Associations between case numbers and university characteristics

A negative binomial count regression model was used to estimate associations between characteristics of higher education settings and the number of COVID-19 cases between 27 September 2021 – 23 February 2022. We made use of publicly available data on university characteristics which could plausibly be associated with transmission. Geographical location and catchment area were included, given the regional variation in prevalence. Presence of a campus and the proportion of students in halls were included as both may have led to denser contact networks and increased mixing. The proportion of students who were undergraduates was included as behaviour and mixing may have feasibly differed from that of postgraduates. The proportion of students who were international students was included as higher numbers may have reflected an increased probability of virus introductions due to overseas travel. We included available data on types of courses offered as these may have been associated with different contact rates among students due to the nature of teaching. These were selected not to provide a comprehensive assessment but as an exploratory component for a potential signal for variance linked to the different courses offered. Membership of the Russell Group of universities was included as a way to group universities which adopted different approaches to control of COVID-19 through increased testing and screening.[27]

During the time period analysed, university campuses remained open (covering the start of the autumn term for the academic year 2021/22 until the end of routine contact tracing). The natural logarithm of the number of registered students (2020/21 academic year, the most recent data available) was used as an offset.

University characteristics were modelled as potential explanatory variables: undergraduate students (percentage of the total number of registered students), international students (percentage of the total number of registered students), the unitary authority catchment (number of unitary authorities from which registered students were drawn, mean-centred), percentage of registered students in halls of residence, and course types offered (medicine and dentistry, creative arts, engineering and technology). The region of the university, Russell group membership, and whether the university was campus-based were also included. Crude associations were estimated using only the variable of interest in the model (with the offset). Associations were described as incidence rate ratios (IRRs).

A negative binomial regression model including all co-variates was used as the starting point for analysis. Improvement of fit to a Poisson model with the same covariables was assessed using a

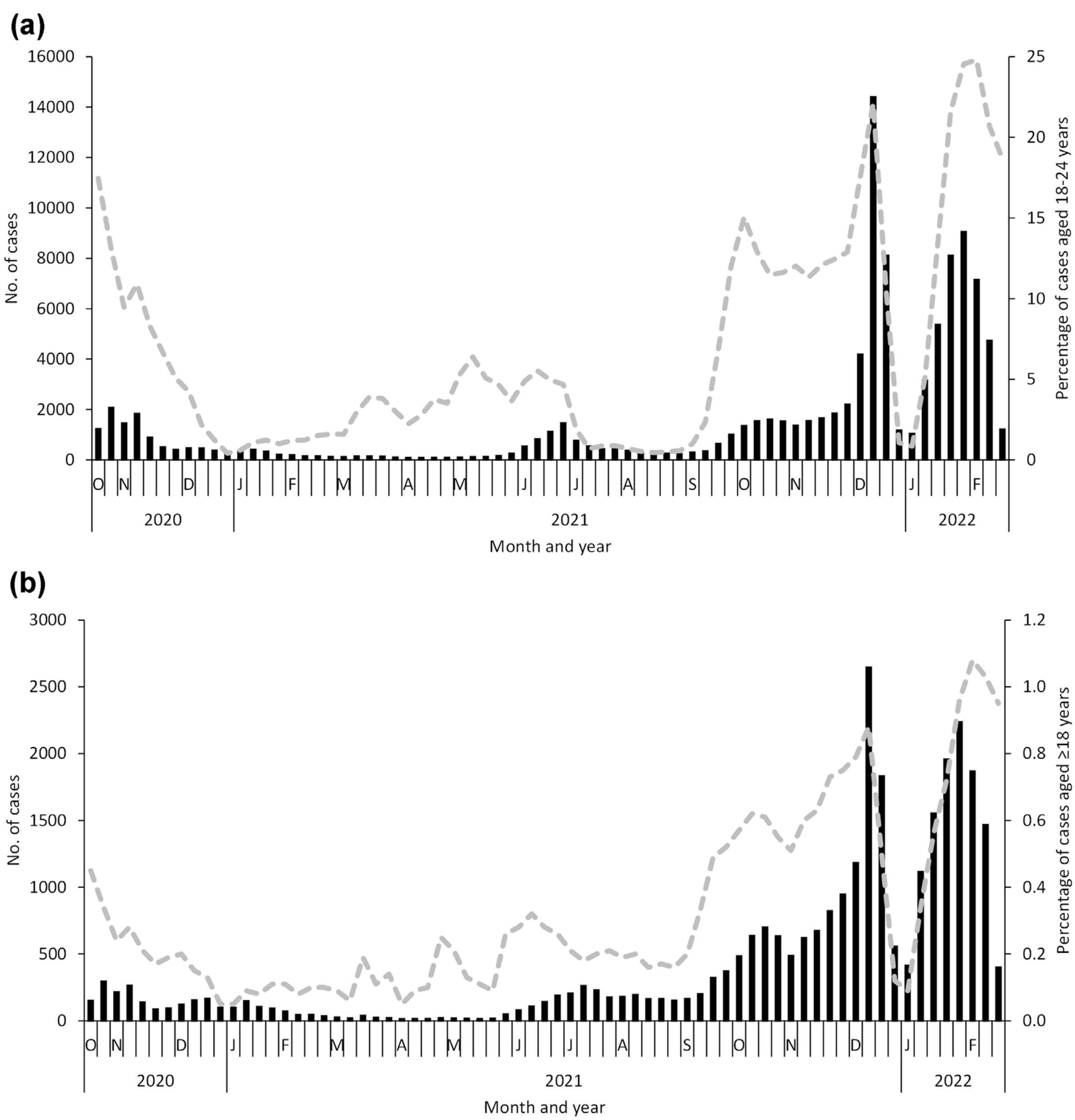

Fig. 1. COVID-19 cases who (a) reported attending university (aged 18–24 years) and (b) reported working at university (aged ≥18 years), October 2020–February 2022, England. Black bars show case numbers aggregated by week of the first reported higher education activity. Grey line indicates case numbers as a percentage of all reported cases for the relevant age group.

likelihood ratio test. The influence of numbers of zero counts was assessed using a zero-truncated negative binomial regression model (using VGAM package in R) with an identical specification compared to the negative binomial model using Akaike Information Criterion (AIC; difference of $\leq$2.5 considered no improvement in fit).[28] Linearity was assessed for continuous variables by modelling variables as quartiles and visually examining estimates across levels.

Plots of standardised deviance residuals against predicted mean and observed values were used to check for outlying residuals. The impact of observations with residuals of values $>\pm2$ was considered by removal of those observations from the model and the change in the IRR and significance noted. Influential observations with a Cook's D distance $\geq$4/n (where n is the number of observations included in the model) were similarly assessed through removal from the final model.

Results

COVID-19 cases associated with higher education settings

Of the individuals who completed contact tracing during the study period, 102,382 were defined as university students and 28,639 as university staff. Student cases were more often female (n = 64,927, 63.4%) with a median age of 21 years (interquartile range [IQR] = 19–35). Staff cases were older (median age: 37, IQR = 26–47) and were slightly more often female than male (15,378; 53.7%).

Trends in COVID-19 cases

Generally, trends in university student cases (aged 18–24 years) and staff reflected a similar pattern in case numbers in the wider population of that age group (Fig. 1). Notable peaks in cases among students occurred during October 2020, June 2021, and December 2021. Using the 2020 population of 18–24-year olds in England (4,709,000) and the number of registered students aged $\leq$24 years (1,517,000), given the equal prevalence to the wider population, it was expected that 32% of COVID-19 cases in that age group should be university students. The observed fraction of cases in this age group remained well below this expected level (Fig. 1). The percentage of all cases aged 18–24 years who were university students reached $\geq$20% during peaks in COVID-19 transmission during the winter of 2021/22. Prior to these peaks, the fraction of 18–24-year-old cases who reported university attendance was very low (<1%) when universities were closed. The phased university reopening in March and May 2021 was accompanied by small peaks in the proportion of cases at universities, but absolute numbers remained extremely low at that time. Cases among staff, and the proportion relative to all cases, were considerably less than those for students, although they exhibited very similar patterns over time.

COVID-19 cases associated with specific universities

Of the 173 universities included in the initial list of institutions, 34 were excluded (outside of England, n = 22; widely-distributed study sites, distance-learning based, or satellite institutions, n = 8; did not award degrees, n = 4). Eighty-eight percent (n = 89,971) of student cases and 88% (n = 25,200) of staff cases could be matched to one of the remaining 139 universities. Of those not matched to a university included in the analysis, 2341 student cases (19% of unmatched cases) and 452 staff cases (13% of unmatched cases) were linked to one of the excluded institutions. The remaining unlinked cases could not be matched due to incomplete details for the setting (students: n = 10,070, 10% of all student cases; staff: n = 2,987, 10% of all staff cases). The matching process was tested by manually checking five sets of 1000 randomly sampled cases and was accurate in 98% of cases. The median number of cases associated with each university during the time period used for modelling (September 2021–February 2022) was 354 (IQR = 125–690).

Characteristics of universities associated with COVID-19 case rates

The final multivariable model included 125 higher education institutions (5 excluded as did not offer undergraduate courses; 9 excluded as HESA data were not available) (Table 1). There were 5 variables significantly associated with numbers of COVID-19 cases (Table 2). Russell group membership, campus universities, and higher proportion of students in halls of residence were all associated with increased case numbers. Increasing unitary authority catchment and offering creative arts classes were associated with reduced case numbers.

The full negative binomial model showed significant improvement of fit compared to a Poisson model ($\chi^2 = 1554.332$, $P < 0.001$)

Table 1
University characteristics of institutions (n = 125) used in multivariable model.

Characteristic	Variable	n (%)	Median (IQR)
Region of institution	East Midlands	9 (7.2)	–
	East of England	9 (7.2)	–
	London	34 (27.2)	–
	North East	5 (4.0)	–
	North West	13 (10.4)	–
	South East	20 (16.0)	–
	South West	12 (8.8)	–
	West Midlands	12 (9.6)	–
	Yorkshire and Humber	12 (9.6)	–
Russell group membership	Yes	20 (16.0)	–
	No	105 (84.0)	–
Campus university	Yes	44 (35.2)	–
	No	81 (64.8)	–
Student make-up	Registered students (n)	–	17,470 (6045–22,155)
	Undergraduate students (%)	–	75.5 (68.1–80.3)
	International students	–	16.8 (8.1–29.2)
	UA catchment	–	82 (74–86)
Students resident in halls[a] (%)	–	–	18.2 (10.2–28.8)
Courses offered	Medicine and dentistry	55 (44.0)	–
	Creative arts	113 (90.4)	–
	Engineering and technology	92 (73.6)	–

IQR = interquartile range; UA = unitary authority.
[a] Provider and private.

Table 2
Associations of university characteristics with COVID-19 cases among students at higher education settings, England, September 2021–February 2022.

Characteristic	Variable	Crude		Adjusted	
		IRR (95% CI)	*P*-value	IRR (95% CI)	*P*-value
Region	East Midlands	1.00	–	1.00	–
	East of England	0.036 (0.026–0.050)	0.828	0.944 (0.669–1.333)	0.746
	London	0.944 (0.634–1.365)	0.770	1.024 (0.741–1.402)	0.880
	North East	0.947 (0.580–1.546)	0.215	0.768 (0.509–1.173)	0.211
	North West	0.695 (0.396–1.259)	0.130	0.818 (0.596–1.117)	0.206
	South East	0.710 (0.452–1.101)	0.893	1.134 (0.845–1.508)	0.397
	South West	1.028 (0.673–1.536)	0.893	1.022 (0.734–1.418)	0.898
	West Midlands	1.131 (0.710–1.784)	0.435	0.989 (0.709–1.372)	0.945
	Yorkshire and Humber	0.834 (0.526–1.310)	0.266	0.843 (0.604–1.174)	0.309
Russell group member	Yes	**1.529 (1.204–1.968)**	**<0.001**	**1.561 (1.220–2.002)**	**<0.001**
	No	1.00	–	–	–
Campus university	Yes	1.088 (0.896–1.327)	0.398	**1.240 (1.055–1.458)**	**0.008**
	No	1.00	–	–	–
Student make-up	Undergraduate students (%)	0.994 (0.987–1.000)	0.064	1.003 (0.995–1.011)	0.466
	International students (%)	**1.011 (1.005–1.018)**	**<0.001**	1.003 (0.995–1.011)	0.450
	UA catchment[b]	**0.995 (0.990–0.999)**	**0.022**	**0.989 (0.982–0.995)**	**<0.001**
Students in halls[a] (%)	–	**1.015 (1.008–1.022)**	**<0.001**	**1.012 (1.004–1.019)**	**0.002**
Courses offered	Medicine and dentistry	1.009 (0.836–1.219)	0.930	0.971 (0.815–1.155)	0.736
	Creative arts	**0.717 (0.541–0.936)**	**0.016**	**0.708 (0.556–0.893)**	**0.004**
	Engineering and technology	**0.775 (0.633–0.945)**	**0.012**	0.925 (0.740–1.153)	0.484

Bold text indicates *P*-values <0.05. IRR = incidence rate ratio; UA = unitary authority.
[a] Provider and private halls of residence.
[b] Mean-centred.

and there was no indication of improved fit using a zero-truncated negative binomial model (Δ AIC = 2.455). All continuous variables showed no substantial evidence of non-linearity of prediction across quartiles (results not shown). Removal of the 9 standardised deviance residuals with a value $>\pm 2$ had very little effect on IRR estimates (average change of 1.3%, range: 0.1–4.5%). Removal of the 4 observations with a Cook's D distance >0.032 also had little impact on IRR estimates (average change of 3.1%, range: 0.1–7.4%).

Discussion

Phased campus reopening in spring 2021 coincided with only a modest increase in COVID-19 case numbers among university students and staff, which remained low until the emergence of the Omicron variant in December 2021. This suggests that preventative actions taken by universities, such as regular screening, support for isolating students, and safety and hygiene measures were successful at minimising transmission of COVID-19. Certainly, student compliance and belief in the importance of such measures was high in the UK[10,29] and could be a key component of successful university interventions.

At no point did the contribution of student cases exceed that expected if there were equivalent prevalence to the wider population of the same age group. Even following the emergence of the Omicron variant in winter of 2021/22 when case rates among young adults were considerably higher than for the Delta variant,[30] this proportion (reaching 20–25% during this time) remained below the expected proportion (32%). This implies a comparatively reduced burden of COVID-19 among students relative to people of their age who were not at the university, and university settings may have generally played a limited role in driving transmission on a wider, population level. Registered university students may, however, have contributed to COVID-19 community transmission when not attending university (such as during the emergence of the Omicron variant in the winter of 2021/22), and the focus of this analysis was restricted to cases associated with higher education settings which were open for teaching.

Our analysis of university-level factors and COVID-19 case rates during winter of 2021/22 indicates that variance in case numbers was associated with a number of university characteristics, some of which may be amenable for targeted interventions or risk communication strategies. Universities with substantial campuses or with large populations of students in halls of residence may be at risk of relatively increased transmission of respiratory viruses. Increased testing rates may equally explain the association with more students in halls, and further work is required to test this. These findings are supported by previous studies linking student accommodation to transmission.[9,10] The association of Russell group membership with increased rates of COVID-19 may reflect increased testing rates at these institutions. Russell group universities were collectively aware of the need for mass testing of students.[27] The greater assets of these major universities may have permitted more resources to be dedicated to student-screening programmes, and consequently, case ascertainment rates were likely higher at some or all of these institutions. The association between reducing case rates and increasing catchment draws of universities requires further investigation and may be confounded by other factors, such as time-specific epidemiology of COVID-19 from the specific areas from which students were drawn. Reduced rates associated with institutions offering creative arts degrees also requires further exploration.

Using routine contact tracing data in England, we have reported cases in university settings for students and staff and described those cases against the backdrop of national case numbers. As was expected, given the fluctuating age-specific transmission rates, national lockdowns, and waves of infection, case numbers among university students varied considerably over time. Substantial variation was also observed between universities, and multivariable modelling highlighted characteristics of universities associated with higher case rates which may help to inform future guidance to limit transmission within higher education settings. Our findings may not be directly comparable with studies undertaken at specific universities in England but provide the first comprehensive overall picture of trends in student case numbers during the pandemic.

Limitations

These findings from real-world data have a number of limitations. A combination of imperfect case ascertainment, particularly for asymptomatic infection,[31] and a lack of engagement with contact tracing, particularly for young people,[32] will have led to an underestimate of case numbers associated with (reported activities at) university settings. An indication of the magnitude of this effect is provided by a comparison of case numbers to those obtained from a mandatory weekly testing programme at Loughborough University (N. Budworth, personal communication). For the period 1 October 2021 to 23 February 2022, cases numbers from contact-tracing data were 37% (1272/1745) and 16% (270/323) lower for students and staff, respectively, than those from the university testing data. Without access to similar testing data at other universities, it was not possible to determine if this under-ascertainment was representative of all other universities. There was likely to be variation between settings due to differential testing and engagement with contact tracing (including reporting of activities leading to linkage to a university setting). The use of routine contact tracing data with sufficient data to allocate cases to university settings limited the analysis to start in October 2020. It is unclear what effects exclusion of the first phase of the pandemic may have had on our findings.

As an ecological study, the findings of this study are largely exploratory; no attempt has been made to consider individual-level factors associated with infection. Linkage of contact tracing data to genomics data may enable detection and description of transmission chains associated with a wider range of higher education settings. The application of such a methodology would allow the degree of intra-university spread and the extent of spillover between university students and wider population groups to be studied over the course of the pandemic and for the whole of England. Our analysis of university characteristics associated with rates of COVID-19 is somewhat crude but suggests potential university-level factors which may have contributed to relatively increased transmission at certain settings. The collection of more detailed data on university environments and student behaviour/mixing over the course of the pandemic would enable factors to be considered at higher resolution and temporal variation in risk modelled. Our analysis of catchment areas has not considered the prevalence of infection within those areas from which students were drawn and the effect this may have had on case numbers.[33]

Author statements

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Ethical approval

The Research Ethics and Governance Group of Public Health England (now UK Health Security Agency) gave ethical approval for this work. R&D reference: R&D 431.

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Competing interests

The authors declare no competing interests.

References

1. Hill EM, Atkins BD, Keeling MJ, Tildesley MJ, Dyson L. Modelling SARS-CoV-2 transmission in a UK university setting. *Epidemics* 2021;**36**:100476.
2. Lopman B, Liu CY, Le Guillou A, Handel A, Lash TL, Isakov AP, et al. A modeling study to inform screening and testing interventions for the control of SARS-CoV-2 on university campuses. *Sci Rep* 2021;**11**(1):5900.
3. Muller K, Muller PA. Mathematical modelling of the spread of COVID-19 on a university campus. *Infect Dis Model* 2021;**6**:1025–45.
4. Office for National Statistics. *How has coronavirus (COVID-19) spread among students in England?*. https://www.ons.gov.uk/peoplepopulationandcommunity/educationandchildcare/articles/howhascoronaviruscovid19spreadamongstudentsinengland/2020-12-21, 2020. [Accessed 29 December 2022].
5. Sample I, Adams R. *Students returning at Christmas could seed new coronavirus outbreaks, scientists warn*. https://www.theguardian.com/education/2020/sep/05/students-returning-at-christmas-could-seed-new-coronavirus-outbreaks-scientists-warn, 2020. [Accessed 29 December 2022].
6. Tidman Z. *Coronavirus: Students breaking social guidelines "on the whole" behind university spikes, minister says*. https://www.independent.co.uk/news/education/education-news/coronavirus-university-students-covid-cases-infections-uk-b834204.html, 2020. [Accessed 29 December 2022].
7. Leeman D, Flannagan J, Chudasama D, Dack K, Anderson C, Dabrera G, et al. Effect of returning university students on COVID-19 infections in England, 2020. *Emerg Infect Dis* 2022;**28**(7):1366–74.
8. Department for Education. *Updated guidance for universities ahead of reopening*. https://www.gov.uk/government/news/updated-guidance-for-universities-ahead-of-reopening, 2020. [Accessed 29 December 2022].
9. Aggarwal D, Warne B, Jahun AS, Hamilton WL, Fieldman T, du Plessis L, et al. Genomic epidemiology of SARS-CoV-2 in a UK university identifies dynamics of transmission. *Nat Commun* 2022;**13**(1):751.
10. Nickbakhsh S, Hughes J, Christofidis N, Griffiths E, Shaaban S, Enright J, et al. Genomic epidemiology of SARS-CoV-2 in a university outbreak setting and implications for public health planning. *Sci Rep* 2022;**12**(1):11735.
11. Department for Education. *Christmas guidance set out for university students*. https://www.gov.uk/government/news/christmasguidance-set-out-for-university-students, 2020. [Accessed 29 December 2022].
12. Hubble S, Bolton P, Lewis J. *Coronavirus: HE/FE return to campus in England 2021*. https://researchbriefings.files.parliament.uk/documents/CBP-9142/CBP-9142.pdf, 2021. [Accessed 29 December 2022].
13. Wathelet M, Fovet T, Jousset A, Duhem S, Habran E, Horn M, et al. Prevalence of and factors associated with post-traumatic stress disorder among French university students 1 month after the COVID-19 lockdown. *Transl Psychiatry* 2021;**11**(1):327.
14. Gullo S, Misici I, Teti A, Liuzzi M, Chiara E. Going through the lockdown: a longitudinal study on the psychological consequences of the coronavirus pandemic. *Res Psychother* 2020;**23**(3):494.
15. Catling JC, Bayley A, Begum Z, Wardzinski C, Wood A. Effects of the COVID-19 lockdown on mental health in a UK student sample. *BMC Psychol* 2022;**10**(1):118.
16. Evans S, Alkan E, Bhangoo JK, Tenenbaum H, Ng-Knight T. Effects of the COVID-19 lockdown on mental health, wellbeing, sleep, and alcohol use in a UK student sample. *Psychiatry Res* 2021;**298**:113819.
17. Owens M, Townsend E, Hall E, Bhatia T, Fitzgibbon R, Miller-Lakin F. Mental Health and wellbeing in young people in the UK during lockdown (COVID-19). *Int J Environ Res Public Health* 2022;**19**(3):1132.
18. Martínez-Lezaun I, Santamaría-Vázquez M, Del Líbano M. Influence of confinement by COVID-19 on the quality of sleep and the interests of university students. *Nat Sci Sleep* 2020;**12**:1075–81.
19. Viselli L, Salfi F, D'Atri A, Amicucci G, Ferrara M. Sleep quality, insomnia symptoms, and depressive symptomatology among Italian university students before and during the Covid-19 Lockdown. *Int J Environ Res Public Health* 2021;**18**(24):13346.
20. Goncalves A, Le Vigouroux S, Charbonnier E. University students' lifestyle behaviors during the COVID-19 pandemic: a four-wave longitudinal survey. *Int J Environ Res Public Health* 2021;**18**(17):8998.
21. Gamage KAA, Pradeep RGGR, Najdanovic-Visak V, Gunawardhana N. Academic standards and quality assurance: the impact of COVID-19 on university degree programs. *Sustainability* 2020;**12**(23):10032.
22. Thatcher A, Zhang M, Todoroski H, Chau A, Wang J, Liang G. Predicting the impact of COVID-19 on Australian universities. *J Risk Financ Manag* 2020;**13**(9):188.
23. The Uni Guide. *What is a campus university? List of campus unis in the UK*. https://www.theuniguide.co.uk/advice/preparing-for-university/list-of-campus-unis-in-the-uk, 2022. [Accessed 29 December 2022].
24. Russell Group. Our universities. https://russellgroup.ac.uk/about/our-universities [Accessed 29 December 2022].
25. Office for Students. *The OfS Register*. https://www.officeforstudents.org.uk/advice-and-guidance/the-register/the-ofs-register/ [Accessed 29 December 2022].
26. R Core Team. *R*: A language and environment for statistical computing (*Version 4.0.3*). https://www.r-project.org/ [Accessed 29 December 2022].

27. Russell Group. Universities' response to Covid-19 – autumn update 2. https://www.russellgroup.ac.uk/news/universities-response-to-covid-19-autumn-update-2/ [Accessed 21 July 2023].
28. Hilbe JM. *Negative binomial regression*. 2nd ed. Cambridge: Cambridge University Press; 2011.
29. Blake H, Knight H, Jia R, Corner J, Morling JR, Denning C, et al. Students' views towards Sars-Cov-2 mass asymptomatic testing, social distancing and self-isolation in a university setting during the COVID-19 pandemic: a qualitative study. *Int J Environ Res Public Health* 2021;**18**(8):4182.
30. Public Health England. SARS-CoV-2 variants of concern and variants under investigation in England. *Technical briefing* 2021;**33**. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1043807/technical-briefing-33.pdf. [Accessed 29 December 2022].
31. Mathers J, Poyner C, Thompson D, Rudge G, Pritchett RV. Exploration of the uptake of asymptomatic COVID-19 lateral flow testing in Birmingham, UK: survey and qualitative research. *BMJ Open* 2022;**12**(4):e056606.
32. Smith LE, Potts HWW, Amlôt R, Fear NT, Michie S, Rubin GJ. Adherence to the test, trace, and isolate system in the UK: results from 37 nationally representative surveys. *BMJ* 2021;**372**:n608.
33. Andersen MS, Bento AI, Basu A, Marsicano CR, Simon KI. College openings in the United States increase mobility and COVID-19 incidence. *PLoS One* 2022;**17**(8):e0272820.

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Original Research

COVID-19 vaccine safety in Scotland – background rates of adverse events of special interest

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ABSTRACT

Objectives: Mass COVID-19 vaccination commenced in December 2020 in Scotland. Monitoring vaccine safety relies on accurate background incidence rates (IRs) for health outcomes potentially associated with vaccination. This study aimed to quantify IRs in Scotland of adverse events of special interest (AESI) potentially associated with COVID-19 vaccination.
Study design and methods: IRs and 95% confidence intervals (CIs) for 36 AESI were calculated retrospectively for the pre-COVID-19 pandemic period (01 January 2015–31 December 2019) and the COVID-19 pandemic period (01 April 2020–30 November 2020), with age-sex stratification, and separately by calendar month and year. Incident cases were determined using International Classification of Diseases-10th Revision (ICD-10)–coded hospitalisations.
Results: Prepandemic population-wide IRs ranged from 0.4 (0.3–0.5 CIs) cases per 100,000 person-years (PYRS) for neuromyelitis optica to 478.4 (475.8–481.0 CIs) cases per 100,000 PYRS for acute renal failure. Pandemic population-wide IRs ranged from 0.3 (0.2–0.5 CIs) cases per 100,000 PYRS for Kawasaki disease to 483.4 (473.2–493.7 CIs) cases per 100,000 PYRS for acute coronary syndrome. All AESI IRs varied by age and sex. Ten AESI (acute coronary syndrome, acute myocardial infarction, angina pectoris, heart failure, multiple sclerosis, polyneuropathies and peripheral neuropathies, respiratory failure, rheumatoid arthritis and polyarthritis, seizures and vasculitis) had lower pandemic than prepandemic period IRs overall. Only deep vein thrombosis and pulmonary embolism had a higher pandemic IR.
Conclusion: Lower pandemic IRs likely resulted from reduced health-seeking behaviours and healthcare provision. Higher IRs may be associated with SARS-CoV-2 infections. AESI IRs will facilitate future vaccine safety studies in Scotland.

Introduction

Infection with severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is associated with high levels of morbidity and mortality.[1] In order to slow the spread of the virus, stringent measures equating to a national lockdown were first introduced in Scotland on 23 March 2020.[2]

Given the severity of the disease (termed COVID-19) and the adverse impact of behavioural restrictions on the economy, several vaccines for COVID-19 were developed rapidly. These were granted emergency use authorisation in the UK, and the COVID-19 vaccination programme in Scotland commenced with the roll-out of the BNT162b2 (Comirnaty) vaccine on 08 December 2020.[3] Although the vaccines passed clinical trials, these are often conducted on populations with limited heterogeneity and follow-up time and without statistical power to detect very rare clinical adverse events associated with vaccination.[4] Therefore, some adverse events may not become apparent until after the vaccine is available to the general population. Health conditions reported or experienced following vaccination can increase vaccine hesitancy and even

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Abbreviations

AESI	Adverse event of special interest
CIs	Confidence intervals
DPIA	Data Protection Impact Assessment
DVT	Deep vein thrombosis
GBS	Guillain-Barre Syndrome
ICD-10	International Classification of Diseases-10th Revision
ICMJE	International Committee for Medical Journal Editors
IR	Incidence rates
MHRA	Medicines and Healthcare products Regulatory Agency
NHS	National Health Service
PE	Pulmonary embolism
PHS	Public Health Scotland
PYRS	Person-years
SARS-CoV-2	Severe acute respiratory syndrome coronavirus-2
SMR01	Scottish Morbidity Record 01
SMR02	Scottish Morbidity Record 02
SPEAC	Safety Platform for Emergency vACcines

result in temporary suspensions to vaccination,[5] requiring investigation to verify whether they are true adverse reactions or are merely temporally associated with vaccination.[6] As such, it is important to continue monitoring potential adverse events to further inform the safety and ensure the credibility of the vaccination programme.

The Brighton Collaboration, an international voluntary collaboration of healthcare professionals currently funded by the Coalition for Epidemic Preparedness Innovation to develop vaccine safety protocols for emerging vaccines,[7] identified a number of health outcomes that could potentially be adverse events associated with COVID-19 vaccination. These are known as adverse events of special interest (AESI).[8] They were identified because they have previously been or theoretically could be associated with vaccination, or because they are associated with COVID-19 disease. Accurate population background rates of AESI are required to monitor vaccine safety.[4] They provide estimates of the incidence of AESI in the absence of the vaccine, so they can be used to estimate the expected incidental rate of AESI in the vaccinated population.[4] Ideally, rates should be from a time period with comparable healthcare use to the period of vaccine administration in the population.[9] If the AESI incidence in the vaccinated population is observed to be higher than the expected rate, this may signal a safety issue for further investigation. Whereas passive surveillance systems, such as the Medicine and Healthcare products Regulatory Agency's (MHRA) Yellow Card Scheme or the US Vaccine Adverse Events Reporting System, rely on voluntary reporting and are most useful for generating hypotheses surrounding potential adverse events following vaccination,[10] background rates facilitate studies that can provide more robust evidence regarding vaccine safety. These, in turn, can improve vaccine confidence and limit vaccine hesitancy.[6]

This study aimed to quantify background incidence rates (IRs) of conditions identified as AESI in the safety monitoring of new COVID-19 vaccinations, including BNT162b2 (Comirnaty), ChAdOx1 nCoV-19 (AZD1222; Vaxzevria) and mRNA-1273 (Spikevax), to inform and enable future vaccine safety analyses.

Methods

Thirty-six AESI were included based on outcomes recommended for monitoring by the Safety Platform for Emergency vACcines (SPEAC) and further informed by discussions with the MHRA and outcomes previously monitored for influenza vaccination.[11] AESI were defined by the International Classification of Diseases-10th Revision (ICD-10)[12] diagnostic codes (Supplemental Table 1) advised by the Public Health Scotland (PHS) terminology service, who routinely validate these codes to ensure they are recorded consistently and accurately.[13] Clinicians within PHS and the University of Glasgow agreed the final selection of AESI and their definitions.

Patients hospitalised with an AESI were identified retrospectively using the Scottish Morbidity Record 01[14] (SMR01) and 02 (SMR02)[15] national data sets. SMR01 includes discharge diagnoses data for all inpatient and day patient episodes from acute specialty hospitals, excluding obstetric and psychiatric specialties. SMR02 includes episode-level data every time a person attends hospital for an obstetric event (antenatal, delivery or postnatal).

Episode-level data were extracted from SMR01 and SMR02 for the period 01 June 2013 to 08 September 2021 and filtered to remove episodes with unknown or unspecified patient sex. An episode is a period of hospital care initiated by a referral or admission and ended by a discharge.[16] AESI events were identified by an ICD-10 code within any diagnosed condition from an episode.[16] The initial data extract covered a longer period than the study periods to account for hospital stays that overlapped with but started or ended outside these dates.

SMR01 episodes were aggregated to hospital stay level for individuals based on their unique Community Health Index number, counting multiple events within a stay once for each AESI. SMR02 data were retained at episode level.

Incident cases were identified using a similar approach to the Centre for Biologics Evaluation and Research.[17] The time between multiple admissions for an individual for the same AESI was calculated using the earliest admission dates from each SMR01 stay and SMR02 episode. AESI events were included if an individual was not previously admitted with a diagnosis of the same AESI within a prespecified time period (clean window). The clean window was verified with clinicians and based on the aetiology of each outcome event (Supplemental Table 1). For example, Guillain-Barre Syndrome's (GBS) clean window was 365 days. For a patient admitted on 01 April 2018 and again on 01 June 2018 with a GBS diagnosis, only the earlier admission was identified as a case (Fig. 1). Individuals contributed multiple incident cases if their events were separated by a period greater than the clean window. The longest clean window was 365 days, so hospitalisations from 01 January 2014 were used to identify incident cases from 01 January 2015 onwards.

For each AESI, IRs per 100,000 PYRS (person-years) and 95% confidence intervals (CIs) were calculated by calendar month and year and overall by age group (0–11, 12–15, 16–19, 20–29, 30–39, 40–49, 50–59, 60–69, 70–79, 80+ years, all ages) and sex (male, female) for two study periods. The pre-COVID-19 pandemic period was 01 January 2015 to 31 December 2019. The COVID-19 pandemic period was 01 April 2020 to 30 November 2020, before the vaccination programme in Scotland started. Denominator data were National Records of Scotland mid-year population estimates.[18] Until the end of March 2020, confirmed COVID-19 infection rates in Scotland were low; therefore, 01 January 2020 to 31 March 2020 was excluded from the prepandemic and pandemic study periods. IRs for this period were calculated separately for information only.

IRs for each AESI were compared between the prepandemic and pandemic periods. IRs were defined as higher where the IR and 95%

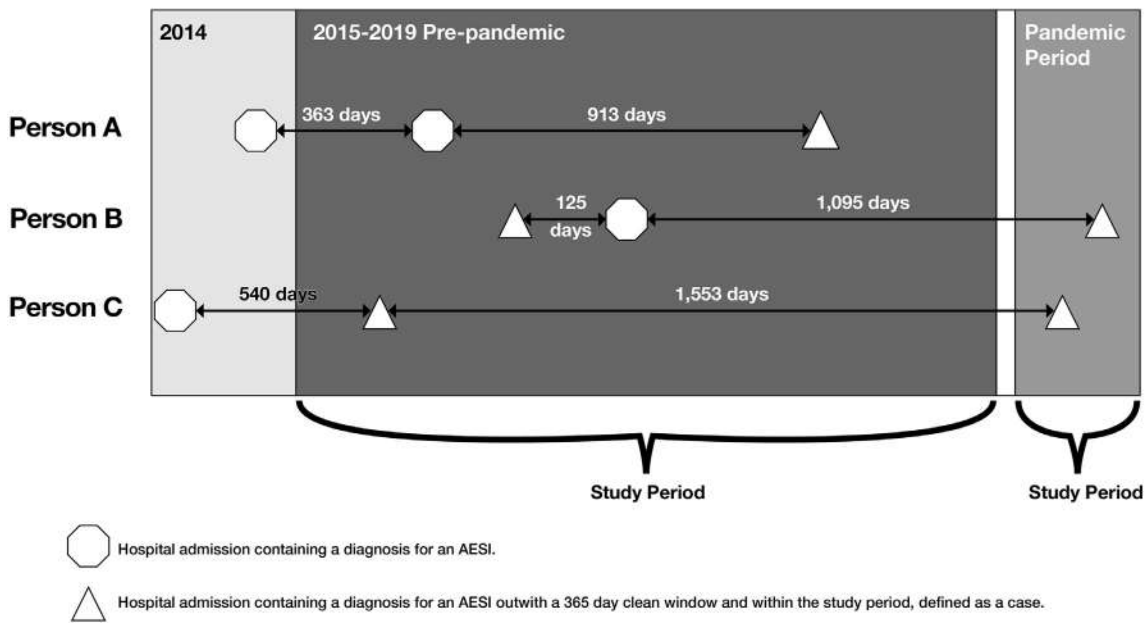

Fig. 1. Identifying cases from three individuals' hospital admissions for Guillain-Barre Syndrome using a 365-day clean window.

CIs were above those of a comparison rate with no overlap between them. The reverse was defined as lower. Comparisons of IRs by calendar month were used to identify seasonal trends. Analyses were conducted in R version 3.6.1, using the tidyverse,[19] lubridate,[20] janitor,[21] epitools[22] and dplyr[23] packages.

Results

Prepandemic period population estimates ranged from 5,373,000 to 5,463,300 (mean = 5,420,780). The pandemic period population estimate was 3,644,000.[18] As expected, IRs varied substantially across the 36 AESI. Prepandemic population-wide IRs (without age or sex stratification) ranged from 0.4 (0.3–0.5 CIs) cases per 100,000 PYRS for neuromyelitis optica to 478.4 (475.8–481.0 CIs) cases per 100,000 PYRS for acute renal failure (Supplemental Figure 1; Supplemental Table 2). Pandemic period population-wide IRs ranged from 0.3 (0.2–0.5 CIs) cases per 100,000 PYRS for Kawasaki disease to 483.4 (473.2–493.7 CIs) cases per 100,000 PYRS for acute coronary syndrome (Supplemental Fig. 2; Supplemental Table 3).

Prepandemic versus pandemic IRs

Deep vein thrombosis (DVT) and pulmonary embolism (PE) was the only AESI with a higher IR during the pandemic period (pandemic period = 101.8 [98.6–105.1 CIs]; prepandemic period = 91.1 [89.9–92.2 CIs] cases per 100,000 PYRS) (Table 1). This was largely driven by the 40- to 69-year-old age groups (Supplemental Table 1; Supplemental Table 2).

Ten AESI (acute coronary syndrome, acute myocardial infarction, angina pectoris, heart failure, multiple sclerosis, polyneuropathies and peripheral neuropathies, respiratory failure, rheumatoid arthritis and polyarthritis, seizures and vasculitis) had lower IRs overall during the pandemic period (Table 1).

Age and sex

Differences occurred in all AESI IRs when age and sex-stratified (Supplemental Figs. 1-2; Supplemental Tables 2-3). In the prepandemic period, there was a sex difference in IRs for 23 AESI, whereby 12 AESI had higher IRs in males (Supplemental Fig. 1; Supplemental Table 2): acute coronary syndrome, acute myocardial infarction, acute renal failure, angina pectoris, GBS, heart failure, myocarditis and pericarditis, other arterial thromboembolism, polyneuropathies and peripheral neuropathies, seizures, stroke (ischemic) and subsequent myocardial infarction. The other 11 AESI had higher overall IRs in females: autoimmune thyroiditis, chronic fatigue syndrome, demyelination, DVT and PE, facial palsy including Bell's palsy, fibromyalgia, multiple sclerosis, optic neuritis, other venous thromboembolism, respiratory failure and rheumatoid arthritis and polyarthritis (Supplemental Fig. 1; Supplemental Table 2). During the pandemic period, six AESI no longer had sex differences observed in the prepandemic period, including five which were previously higher in females (DVT and PE, facial palsy including Bell's palsy, optic neuritis, other venous thromboembolism, rheumatoid arthritis and polyarthritis), and one that was higher in males (subsequent myocardial infarction).

For most AESI, sex differences varied across age groups except for autoimmune thyroiditis where the IR was consistently higher in females, and seizures where the IR was consistently higher in males (Supplemental Fig. 1, Supplemental Table 2). This pattern was observed in both study periods.

Kawasaki disease and vasculitis were the only AESI predominantly seen in children aged under 12 years for both sexes in both study periods (Figs. 1 and 2; Supplemental Tables 2-3). This pattern was less apparent in the pandemic period for both AESI due to a smaller number of events resulting in wider CIs.

Seasonal trends

Respiratory failure and vasculitis had seasonal trends in both study periods, with higher IRs during winter months (Supplemental Fig. 3; Supplemental Table 4).

Discussion

Estimated IRs from hospitalisations for 36 AESI potentially related to COVID-19 vaccination provide important contextual

Table 1
IRs and 95% CIs of AESI throughout the prepandemic and pandemic periods.

AESI	2015	2016	2017	2018	2019	Prepandemic period (2015–2019 average)	Pandemic period (01 April 2020 to 30 November 2020)
Acute and Subacute Hepatic Failure	2.9 (2.4–3.4)	3.0 (2.6–3.5)	3.2 (2.7–3.7)	3.7 (3.2–4.3)	3.6 (3.1–4.1)	3.3 (3.1–3.5)	3.6 (3.1–4.3)
Acute Coronary Syndrome	454.9 (449.2–460.6)	442.9 (437.3–448.5)	445.9 (440.3–451.6)	434.1 (428.6–439.7)	443 (437.4–448.6)	444.1 (441.6–446.6)	394.4 (388–400.9)
Acute Myocardial Infarction	202.3 (198.5–206.1)	204.4 (200.6–208.2)	205.3 (201.5–209.1)	201.6 (197.9–205.4)	203.0 (199.2–206.8)	203.3 (201.6–205)	192.0 (187.5–196.5)
Acute Renal Failure	433.4 (427.8–439.0)	483.6 (477.8–489.5)	499.8 (493.9–505.8)	487.6 (481.7–493.5)	487.1 (481.3–493.0)	478.4 (475.8–481)	449.8 (442.9–456.7)
Angina Pectoris	278.7 (274.3–283.2)	263.3 (259.0–267.7)	256.0 (251.8–260.3)	243.4 (239.2–247.6)	248.8 (244.6–253.0)	258.0 (256.1–259.9)	211.6 (206.9–216.3)
Autoimmune Thyroiditis	2.9 (2.5–3.4)	3.0 (2.6–3.5)	2.9 (2.5–3.4)	3.9 (3.4–4.4)	3.5 (3.1–4.1)	3.3 (3–3.5)	3.1 (2.5–3.7)
Chronic Fatigue Syndrome	5.5 (4.9–6.1)	5.7 (5.1–6.4)	4.7 (4.2–5.3)	4.3 (3.8–4.9)	4.2 (3.7–4.8)	4.9 (4.6–5.2)	4.0 (3.4–4.7)
Demyelination	2.8 (2.4–3.3)	2.5 (2.1–3.0)	2.8 (2.4–3.3)	2.6 (2.2–3.1)	2.2 (1.8–2.6)	2.6 (2.4–2.8)	2.4 (1.9–2.9)
Disseminated Intravascular Coagulation	1.2 (0.9–1.5)	1.1 (0.8–1.4)	0.9 (0.7–1.2)	0.9 (0.7–1.2)	0.8 (0.6–1.1)	1.0 (0.8–1.1)	1.3 (0.9–1.7)
Deep Vein Thrombosis (DVT) and Pulmonary Embolism (PE)	85.8 (83.4–88.3)	88.9 (86.4–91.5)	93.7 (91.2–96.3)	93.2 (90.6–95.8)	93.6 (91.1–96.2)	91.1 (89.9–92.2)	101.8 (98.6–105.1)
Encephalitis including Acute Disseminated Encephalomyelitis (ADEM)	3.6 (3.1–4.1)	3.3 (2.8–3.8)	3.5 (3.0–4.0)	3.5 (3.1–4.1)	3.6 (3.1–4.1)	3.5 (3.3–3.7)	2.6 (2.1–3.2)
Facial Palsy including Bell's Palsy	15.0 (14.0–16.1)	14.8 (13.8–15.9)	13 (12.0–14.0)	13.4 (12.5–14.5)	13.8 (12.8–14.8)	14.0 (13.6–14.5)	10.9 (9.9–12.1)
Fibromyalgia	34.2 (32.7–35.8)	37.4 (35.8–39.0)	38.0 (36.4–39.6)	44.1 (42.3–45.9)	49.8 (47.9–51.7)	40.7 (40–41.5)	47.5 (45.3–49.8)
Guillain-Barre Syndrome (GBS)	3.0 (2.5–3.5)	3.2 (2.7–3.7)	3 (2.5–3.5)	2.7 (2.3–3.2)	2.9 (2.5–3.4)	2.9 (2.7–3.2)	2.3 (1.8–2.8)
Heart Failure	259.0 (254.7–263.3)	263.5 (259.2–267.8)	269.4 (265.1–273.8)	264.7 (260.4–269.1)	277.5 (273.1–282.0)	266.9 (264.9–268.8)	249.0 (243.9–254.2)
Intracranial Venous Thrombosis	1.2 (0.9–1.5)	1.6 (1.3–2.0)	1.5 (1.2–1.9)	1.9 (1.5–2.3)	1.7 (1.4–2.1)	1.6 (1.4–1.7)	1.8 (1.4–2.3)
Kawasaki Disease	0.4 (0.3–0.6)	0.4 (0.2–0.5)	0.5 (0.3–0.7)	0.6 (0.4–0.9)	0.5 (0.4–0.8)	0.5 (0.4–0.6)	0.3 (0.2–0.5)
Multiple Sclerosis	35.8 (34.2–37.5)	35.5 (34.0–37.2)	36.3 (34.7–37.9)	38.8 (37.2–40.5)	37.3 (35.7–39.0)	36.8 (36–37.5)	31.3 (29.5–33.2)
Myasthenia Gravis	5.0 (4.4–5.7)	5.4 (4.8–6.1)	5.5 (4.9–6.2)	5.6 (5.0–6.3)	6.1 (5.5–6.8)	5.5 (5.3–5.8)	4.6 (4–5.4)
Myocarditis and Pericarditis	7.8 (7.1–8.6)	7.1 (6.4–7.8)	7.8 (7.1–8.6)	8.7 (7.9–9.5)	9 (8.2–9.8)	8.1 (7.7–8.4)	8.9 (8–9.9)
Narcolepsy	0.7 (0.5–0.9)	0.6 (0.4–0.9)	0.6 (0.4–0.9)	0.5 (0.3–0.7)	0.5 (0.3–0.7)	0.6 (0.5–0.7)	0.5 (0.3–0.8)
Neuromyelitis Optica	0.3 (0.1–0.4)	0.5 (0.3–0.7)	0.3 (0.2–0.5)	0.4 (0.2–0.6)	0.6 (0.4–0.8)	0.4 (0.3–0.5)	0.5 (0.3–0.8)
Optic Neuritis	1.8 (1.4–2.2)	1.9 (1.6–2.4)	1.2 (1.0–1.6)	1.8 (1.5–2.2)	1.8 (1.4–2.2)	1.7 (1.6–1.9)	1.2 (0.9–1.6)
Other Arterial Thromboembolism	21.7 (20.5–23.0)	22.5 (21.3–23.8)	25.5 (24.2–26.9)	25.9 (24.6–27.3)	24.8 (23.5–26.2)	24.1 (23.5–24.7)	20.6 (19.2–22.2)
Other Venous Thromboembolism	23.3 (22.1–24.7)	24.1 (22.8–25.4)	24.3 (23.0–25.7)	23.2 (21.9–24.5)	25.9 (24.6–27.3)	24.2 (23.6–24.8)	22.1 (20.6–23.7)
Polyneuropathies and Peripheral Neuropathies	33.4 (31.9–35.0)	34.8 (33.3–36.5)	33.7 (32.2–35.3)	33.3 (31.8–34.9)	34.9 (33.3–36.5)	34.0 (33.3–34.7)	27.0 (25.3–28.7)
Respiratory Failure	69.5 (67.3–71.8)	78.4 (76.1–80.8)	84.8 (82.3–87.2)	82.4 (80.0–84.8)	83.4 (81.0–85.8)	79.7 (78.6–80.8)	56.4 (54–58.9)
Rheumatoid Arthritis and Polyarthritis	80.5 (78.1–82.9)	75.5 (73.2–77.8)	72.7 (70.5–75.0)	71.4 (69.2–73.7)	73.3 (71.0–75.6)	74.7 (73.6–75.7)	50.1 (47.9–52.5)
Seizures	338.8 (333.9–343.8)	347.9 (343.0–352.9)	347.6 (342.7–352.6)	340.8 (335.9–345.8)	353.8 (348.8–358.8)	345.8 (343.6–348)	299.5 (293.9–305.2)
Stroke (Haemorrhagic)	48.9 (47.0–50.8)	49.9 (48.0–51.8)	48.0 (46.2–49.9)	50.3 (48.4–52.2)	51.1 (49.2–53.0)	49.6 (48.8–50.5)	46.6 (44.4–48.8)
Stroke (Ischemic)	181.1 (177.5–184.7)	181.5 (177.9–185.1)	184.3 (180.7–188.0)	183.9 (180.4–187.6)	185.4 (181.8–189.1)	183.3 (181.7–184.9)	182.5 (178.1–186.9)
Subsequent Myocardial Infarction	3.5 (3.0–4.0)	2.8 (2.3–3.2)	2.3 (1.9–2.7)	2.5 (2.1–3.0)	2.5 (2.1–2.9)	2.7 (2.5–2.9)	2.5 (2–3.1)
Thrombocytopenia	34.7 (33.2–36.3)	33.7 (32.2–35.3)	33 (31.5–34.5)	31.2 (29.7–32.7)	32.7 (31.2–34.2)	33.1 (32.4–33.7)	28.5 (26.8–30.3)
Transient Ischaemic Attack	52.5 (50.6–54.5)	55.7 (53.8–57.8)	59.9 (57.9–62.0)	59.5 (57.4–61.5)	63.1 (61.0–65.3)	58.2 (57.3–59.1)	54.1 (51.7–56.5)
Transverse Myelitis	0.6 (0.4–0.9)	0.7 (0.5–1.0)	0.8 (0.5–1.0)	0.8 (0.6–1.0)	0.6 (0.4–0.9)	0.7 (0.6–0.8)	0.9 (0.6–1.2)
Vasculitis	8.0 (7.3–8.8)	9.7 (8.9–10.5)	8.2 (7.5–9.0)	8.4 (7.6–9.2)	8.2 (7.5–9.0)	8.5 (8.2–8.9)	5.0 (4.3–5.8)

information for monitoring and providing reassurance regarding vaccine safety. If concerns around serious adverse events occurring post-vaccination are reported through social media, passive reporting or anecdotally, these estimates facilitate quick comparisons of observed number of events in the vaccinated population with the expected number of events. Lower event rates among vaccinees than the background rates provide reassurance that events may have occurred coincidentally. However, it is important that background rates used reflect the IRs of AESI in the absence of vaccination as closely as possible.

Ten AESI (acute coronary syndrome, acute myocardial infarction, angina pectoris, heart failure, multiple sclerosis, polyneuropathies and peripheral neuropathies, respiratory failure, rheumatoid arthritis and polyarthritis, seizures and vasculitis) had lower IRs following the emergence of COVID-19 and associated behavioural restrictions (Table 1; Supplemental Figure 3). To our knowledge, this study is the first to examine changes in IRs for polyneuropathies and peripheral neuropathies and vasculitis following the COVID-19 pandemic. However, findings for the remaining eight AESI that had lower pandemic period IRs align with other studies examining the same conditions.[24–28]

Reasons for observing lower pandemic period IRs are likely to be multifactorial. These are important to consider when choosing comparison periods for vaccine safety analyses. Several studies have attributed reduced IRs to health-seeking behaviour changes during the pandemic, suggesting anxiety around SARS-CoV-2 infection may prevent or delay presentation at hospital, particularly during the early pandemic period.[24,28,29] This was evidenced by research showing decreased self-referrals but increased ambulance admissions to hospital with heart failure during 2020 compared with prior years.[30] These findings indicate a shift in patients seeking medical care only for more serious events during the pandemic rather than a true reduction in IRs.

Lower pandemic IRs are also likely caused by the National Health Service (NHS) being placed on emergency footing from 17 March 2020.[31] Many healthcare services were paused to allocate resources to managing COVID-19 cases. This affected referral and treatment patterns, and all non-urgent elective treatment was suspended. Indeed, several AESI that were lower during the pandemic were related to the circulatory system (acute coronary syndrome, acute myocardial infarction, heart failure, angina pectoris, vasculitis). Elective cardiac surgery and cardiology were among the paused services, and their staged return only began mid-June 2020.[32] Accordingly, we observed that most AESI with lower pandemic IRs gradually increased throughout the pandemic period, returning to levels more closely resembling prepandemic IRs around the same time NHS services recommenced (Supplemental Figure 3). Similarly, community deaths from heart failure were higher and hospitalisations were lower during the period February to May 2020 compared with equivalent 2018 and 2019 time periods in England.[29] Other factors causing reduced IRs could include individuals practicing better self-care over the pandemic period[33] if they had more available time compounded with the incentive to stay healthy in case of SARS-CoV-2 infection. For others, reduced physical activity due to behavioural restrictions could have masked the symptoms from cardiovascular AESI,[34] meaning individuals were less aware of a need to attend hospital.

Reduced physical activity may have also contributed to the observed increased rates of DVT and PE during the pandemic period.[34] It is also notable that SARS-CoV-2 infection has been associated with PE and may therefore have increased relative to increasing infection rates.[35] Although DVT and PE was the only AESI that was higher overall during the pandemic than prepandemic period, rates of several other AESI (including acute renal failure, GBS, disseminated intravascular coagulation) were also likely affected during the pandemic given their association with COVID-19.[36–38]

Consistent with other research, IRs varied substantially by age and sex.[21] Generally, IRs were highest in adults across both prepandemic and pandemic periods (Supplemental Fig. 1; Supplemental Fig. 2). Exceptions were Kawasaki disease and vasculitis where IRs were highest in under 12-year-olds in the prepandemic period. The majority of AESI also had higher IRs in one sex during the prepandemic period (Supplemental Fig. 1). Prepandemic IRs for acute myocardial infarction, myocarditis and pericarditis and GBS were higher in males than females, matching findings in a UK study of IRs from 2017 to 2019.[21] However, sex differences in general were less apparent during the pandemic period (Supplemental Fig. 2). For some AESI, including thrombocytopenia, sex differences were age-dependent such that the IR was higher in younger females than males, but the reverse occurred in older age groups.

For certain conditions, substantial differences in IRs occur throughout the year due to the seasonal nature of the disease, which needs to be considered and accounted for when undertaking safety analyses.[39] Winter peaks observed for respiratory failure in both prepandemic and pandemic periods align with the influenza season (Supplemental Figure 3).[40,41] The marked reduction in respiratory failure throughout the pandemic period (Table 1; Supplemental Figure 3) mirrors the reduction observed in non-COVID-19 respiratory pathogens circulating throughout the pandemic.[41] The lower incidence has been attributed to COVID-19 behavioural restrictions, which prevented the usual transmission of infection observed in previous years.[41]

The study included many AESI identified as relevant to the COVID-19 vaccination programme. By using national data and standardised definitions for identifying AESI, IRs are likely to be reflective of and generalisable to the Scottish population. SMR records are produced for all inpatients and day cases in Scotland and are therefore unbiased towards particular geographical areas or other subsets of patients that may influence IRs. Furthermore, AESI were identified from all episodes within a hospital stay. This increased the likelihood of including stays involving an AESI regardless of severity. The use of a clean window, defined accordingly for each AESI, limited the possibility of identifying repeat admissions for individuals with a history of the condition.

The provision of age and sex-stratified rates will allow future studies to rapidly assess vaccine safety in specific cohorts. By calculating prepandemic and pandemic IRs separately, the pandemic's impact on the incidence of AESI can also be reviewed. This will be particularly important when selecting comparison periods for and interpretation of follow-up vaccine safety analysis. The availability of AESI IRs and the insights into the pandemic's influence and seasonal trends provided will also aid safety studies for other vaccine programmes, such as influenza, and support public health planning in the event of potential future pandemics.[39]

Study limitations

For some AESI, hospitalisation may be unnecessary, and patients are seen in primary care or outpatient settings instead, so they are not counted in IRs. Additionally, some individuals may not seek healthcare, or their hospitalisation might differ based on age, sex or other risk factors for serious disease or complications. While this may have been a particular bias throughout the pandemic period, the data presented likely underestimate the true IRs for some or all conditions across both study periods. Although many AESI were included, the list was not exhaustive, and other adverse events may emerge as safety concerns associated with COVID-19 vaccination. Identification of hospitalisations for the included AESI may have also been affected if any changes occurred to the ICD-10 codes used during the study periods. The clean window length chosen for each AESI will also have influenced IRs, potentially underestimating admissions counted as cases.

2020 mid-year population estimates were also likely affected by higher mortality rates caused by SARS-CoV-2 infections,[42] resulting in the denominator overestimating the true population. Furthermore, excess deaths may have occurred among cohorts most at risk for the AESI investigated. Combined, these could have resulted in lower IRs throughout the pandemic period without any true change in incidence.

Caution should be applied when comparing IRs calculated using different methods and/or databases and from different geographical areas. For example, our prepandemic IR of 2.9 GBS cases per 100,000 PYRS (2.7–3.2 CIs) is higher than UK-wide estimates from 2016 to 2019 calculated using prescriptions of intravenous immunoglobulin for treating GBS in hospital.[43] Our study identified any condition that develops during a stay or affects a patient's management, so it may have included patients with a GBS diagnosis that never received specific GBS treatment. Furthermore, IRs can vary substantially across data sources even when controlling for other confounders.[44] Future research using the IRs made available here should ideally use the same SMR data sets to calculate postvaccination IRs of AESI.

Conclusion

Estimates are provided for potential AESI identified for monitoring in relation to COVID-19 vaccine safety. The findings presented illustrate the effect of age, sex and time period on AESI incidence, which must be considered in future analysis. Appropriately stratified IRs provided will enable rapid assessment of vaccine safety in Scotland, for example in observed versus expected studies, which monitor IRs postvaccination to signal potential safety concerns. Such analyses are commonly used in vaccine vigilance when quick decision-making is required, and reviewing large case numbers individually would be inefficient. This enables public confidence in vaccination to be maintained. The IRs also provide insight into behaviour changes (i.e. likelihood of visiting hospital and being admitted) and the possible impact of COVID-19 on health when comparing prepandemic and pandemic periods.

Author statements

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Author contributions

All listed authors meet the criteria for authorship set forth by the International Committee for Medical Journal Editors (ICMJE). MCO conceived and designed the study and supported the conduct of the analysis. LAC, KA and LW conducted the data analysis. LAC produced the data visualisations. LAC, ZG, KA, CLG, LEM, MSA and MCO contributed to the interpretation of results. LAC drafted and revised the manuscript. In addition, all authors provided revisions to manuscript drafts and guidance throughout the analysis and paper writing process. All authors have read and approved the final manuscript and agree for it to be published.

Ethical approval

The Public Health Scotland Order 2019 in Article 9 (2)(i) places an obligation on Public Health Scotland to engage in the control of the spread of infectious diseases in accordance with section 43 of the National Health Service (Scotland) Act 1978. In accordance with Sections 15, 16 (5), and 21 (2) of the Public Health etc. (Scotland) Act 2008, PHS is obliged to process data in relation to notifiable diseases, health risk states of patients, notifiable organisms, and carrying out public health investigations, and as such, individual patient consent is not required. A Data Protection Impact Assessment (DPIA) allows Public Health Scotland staff to link existing data sets. This study was approved under COVID-19 Rapid DPIA 2122-0077.

Consent for publication

Not applicable.

Availability of data and materials

All data generated during this study are included in this published article and its supplementary information files. R scripts used to produce supplementary figures 1-3 will be made available on GitHub upon publication. Please contact the corresponding author (LEM) for assistance accessing these.

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Not applicable.

Competing interests

The authors declare that they have no competing interests.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.puhe.2023.08.006.

References

1. Kang SJ, Jung SI. Age-related morbidity and mortality among patients with COVID-19. *Infect Chemother* 2020;**52**(2):154–64. Jun 12.
2. Timeline of Coronavirus (COVID-19) in Scotland – SPICe Spotlight | Solas air SPICe [Internet]. [cited 2022 Jan 24]. Available from: https://spice-spotlight.scot/2022/01/21/timeline-of-coronavirus-covid-19-in-scotland/.
3. First COVID-19 vaccinations in Scotland take place. - gov.scot [Internet]. [cited 2022 Jan 31]. Available from: https://www.gov.scot/news/first-covid-19-vaccinations-in-scotland-take-place/.
4. Black SB, Law B, Chen RT, Dekker CL, Sturkenboom M, Huang W-T, et al. The critical role of background rates of possible adverse events in the assessment of COVID-19 vaccine safety. *Vaccine* 2021 May 6;**39**(19):2712–8.
5. Wise J. Covid-19: European countries suspend use of Oxford-AstraZeneca vaccine after reports of blood clots. Mar 11 *BMJ* 2021;**372**. n699.
6. Marti M, de Cola M, MacDonald NE, Dumolard L, Duclos P. Assessments of global drivers of vaccine hesitancy in 2014-Looking beyond safety concerns. *PLoS One* 2017;**12**(3):e0172310. Mar 1.
7. Brighton Collaboration – Home Page - Brighton Collaboration [Internet]. [cited 2022 May 4]. Available from: https://brightoncollaboration.us/.
8. COVID-19 - Brighton Collaboration [Internet]. [cited 2022 Apr 6]. Available from: https://brightoncollaboration.us/covid-19/.
9. Hampton LM, Aggarwal R, Evans SJW, Law B. General determination of causation between Covid-19 vaccines and possible adverse events. *Vaccine* 2021;**39**(10):1478–80. Mar 5.
10. Shimabukuro TT, Nguyen M, Martin D, DeStefano F. Safety monitoring in the vaccine adverse event reporting system (VAERS). *Vaccine* 2015;**33**(36):4398–405. Aug 26.
11. Simpson CR, Lone N, Kavanagh K, Ritchie LD, Robertson C, Sheikh A, et al. *Seasonal Influenza Vaccine Effectiveness (SIVE): an observational retrospective cohort study – exploitation of a unique community-based national-linked database to determine the effectiveness of the seasonal trivalent influenza vaccine*. Southampton (UK): NIHR Journals Library; 2013.

12. ICD-10 Version:2019 [Internet]. [cited 2022 Jan 24]. Available from: https://icd.who.int/browse10/2019/en.
13. ISD Services | Terminology Services and Clinical Coding | Coding & Terminology Systems | ISD Scotland [Internet]. [cited 2023 Jul 20]. Available from: https://www.isdscotland.org/Products-and-Services/Terminology-Services/.
14. SMR Datasets | SMR01 - General/Acute Inpatient and Day Case | ISD Scotland | Data Dictionary [Internet]. [cited 2022 Mar 21]. Available from: https://www.ndc.scot.nhs.uk/Data-Dictionary/SMR-Datasets/SMR01-General-Acute-Inpatient-and-Day-Case/.
15. SMR Datasets | SMR02 - Maternity Inpatient and Day Case | ISD Scotland | Data Dictionary [Internet]. [cited 2022 Mar 21]. Available from: https://www.ndc.scot.nhs.uk/Data-Dictionary/SMR-Datasets/SMR02-Maternity-Inpatient-and-Day-Case/.
16. ISD Scotland | Information Services Division [Internet]. [cited 2022 Jan 26]. Available from: https://www.ndc.scot.nhs.uk/Dictionary-A-Z/Definitions/index.asp?Search=E&ID=241&Title=Episode%20of%20Care.
17. Vaccines & Allergenics – BEST Initiative [Internet]. [cited 2022 Mar 21]. Available from: https://www.bestinitiative.org/vaccines-and-allergenics.
18. Mid-Year Population Estimates | National Records of Scotland [Internet]. [cited 2022 Jan 24]. Available from: https://www.nrscotland.gov.uk/statistics-and-data/statistics/statistics-by-theme/population/population-estimates/mid-year-population-estimates.
19. Wickham H, Averick M, Bryan J, Chang W, McGowan L, François R, et al. Welcome to the tidyverse. *JOSS* 2019;**4**(43):1686.
20. Grolemund G, Wickham H. Dates and times made easy with lubridate. *J Stat Softw* 2011;**40**(3).
21. Firke S. *Simple tools for examining and cleaning dirty data [R package janitor version 2.1.0*. 2021. Jan 5.
22. Aragon TJ. *Epidemiology Tools [R package epitools version 0.5-10.1*. 2020. Mar 22.
23. A Grammar of Data Manipulation [R package dplyr version 1.0.8] [Internet]. 2022 [cited 2022 Mar 21]. Available from: https://cran.r-project.org/web/packages/dplyr/index.html.
24. Leung WCY, Lau EHY, Kwan P, Chang RS-K. Impact of COVID-19 on seizure-related emergency attendances and hospital admissions - a territory-wide observational study. *Epilepsy Behav* 2021;**115**:107497. Feb.
25. He L, Lu F, Du X, Long D, Sang C, Tang R, et al. Impact of COVID-19 pandemic on hospital admissions of acute coronary syndrome: A Beijing inpatient database study. *Lancet Reg Health West Pac* 2022;**19**:100335. Feb.
26. Bodilsen J, Nielsen PB, Søgaard M, Dalager-Pedersen M, Speiser LOZ, Yndigegn T, et al. Hospital admission and mortality rates for non-covid diseases in Denmark during covid-19 pandemic: nationwide population based cohort study. May 24 *BMJ* 2021;**373**. n1135.
27. Frankfurter C, Buchan TA, Kobulnik J, Lee DS, Luk A, McDonald M, et al. Reduced rate of hospital presentations for heart failure during the COVID-19 pandemic in Toronto, Canada. *Can J Cardiol* 2020;**36**(10):1680–4. Oct.
28. Richter D, Faissner S, Bartig D, Tönges L, Hellwig K, Ayzenberg I, et al. The impact of the COVID-19 pandemic on hospitalizations and plasmapheresis therapy in multiple sclerosis and neuromyelitis optica spectrum disorder: a nationwide analysis from Germany. *Ther Adv Neurol Disord* 2021;**14**: 17562864211030656. Jul 7.
29. Severino P, D'Amato A, Saglietto A, D'Ascenzo F, Marini C, Schiavone M, et al. *Reduction in heart failure hospitalization rate during coronavirus disease 19 pandemic outbreak*. ESC Heart Fail; 2020. Oct 23.
30. Kubica J, Ostrowska M, Stolarek W, Kasprzak M, Grzelakowska K, Kryś J, et al. *Impact of COVID-19 pandemic on acute heart failure admissions and mortality: a multicentre study (COV-HF-SIRIO 6 study)*. ESC Heart Fail; 2021.
31. NHS Scotland placed on emergency footing - gov.scot [Internet]. [cited 2022 Mar 11]. Available from: https://www.gov.scot/news/nhs-scotland-placed-on-emergency-footing/.
32. Restarting more health services - gov.scot [Internet]. [cited 2022 Mar 11]. Available from: https://www.gov.scot/news/restarting-more-health-services/.
33. Chang Y-K, Hung C-L, Timme S, Nosrat S, Chu C-H. Exercise behavior and mood during the COVID-19 pandemic in Taiwan: lessons for the future. *Int J Environ Res Public Health* 2020;(19):17.
34. Sokolski M, Gajewski P, Zymliński R, Biegus J, Berg JMT, Bor W, et al. Impact of coronavirus disease 2019 (COVID-19) outbreak on acute admissions at the emergency and cardiology departments across Europe. *Am J Med* 2021;**134**(4): 482–9. Apr.
35. Salihi S, Perçin B, Erkengel HI, Özalp B, Saçlı H, Kara I. Does COVID-19 infection increase the risk of pulmonary embolism in ambulatory patients with deep vein thrombosis. *Vascular* 2021:17085381211052207. Dec 4.
36. Raza A, Estepa A, Chan V, Jafar MS. Acute renal failure in critically ill COVID-19 patients with a focus on the role of renal replacement therapy: a review of what we know so far. *Cureus* 2020;**12**(6):e8429. Jun 3.
37. Caress JB, Castoro RJ, Simmons Z, Scelsa SN, Lewis RA, Ahlawat A, et al. COVID-19-associated Guillain-Barré syndrome: the early pandemic experience. *Muscle Nerve* 2020;**62**(4):485–91. Oct.
38. Mortus JR, Manek SE, Brubaker LS, Loor M, Cruz MA, Trautner BW, et al. Thromboelastographic results and hypercoagulability syndrome in patients with coronavirus disease 2019 who are critically ill. *JAMA Netw Open* 2020;**3**(6):e2011192. Jun 1.
39. Black S, Eskola J, Siegrist C-A, Halsey N, MacDonald N, Law B, et al. Importance of background rates of disease in assessment of vaccine safety during mass immunisation with pandemic H1N1 influenza vaccines. *Lancet* 2009;**374**(9707): 2115–22. Dec 19.
40. The flu vaccine | The flu vaccine [Internet]. [cited 2022 Mar 11]. Available from: https://www.nhsinform.scot/flu-vaccine/the-vaccines/the-flu-vaccine/.
41. HPS weekly national seasonal respiratory report.
42. Deaths involving coronavirus (COVID-19) in Scotland | National Records of Scotland [Internet]. [cited 2022 Feb 21]. Available from: https://www.nrscotland.gov.uk/statistics-and-data/statistics/statistics-by-theme/vital-events/general-publications/weekly-and-monthly-data-on-births-and-deaths/deaths-involving-coronavirus-covid-19-in-scotland.
43. Keddie S, Pakpoor J, Mousele C, Pipis M, Machado PM, Foster M, et al. Epidemiological and cohort study finds no association between COVID-19 and Guillain-Barré syndrome. *Brain* 2021;**144**(2):682–93. Mar 3.
44. Li X, Ostropolets A, Makadia R, Shoaibi A, Rao G, Sena AG, et al. Characterising the background incidence rates of adverse events of special interest for covid-19 vaccines in eight countries: multinational network cohort study. *BMJ* 2021: n1435. Jun 14.

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Original Research

Discretion in decision to receive COVID-19 vaccines and associated socio-economic inequalities in rates of uptake: a whole-of-population data linkage study from Australia

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ABSTRACT

Objective: In Australia, first and second compared to third dose of a COVID-19 vaccine were implemented under different policies and contexts, resulting in greater discretion in decisions to receive a third compared to first and second dose. We quantified socio-economic inequalities in first and third dose to understand how discretion is associated with differences in uptake.
Study design: Whole-of-population cohort study.
Methods: Linked immunisation, census, death and migration data were used to estimate weekly proportions who received first and third doses of a COVID-19 vaccine until 31 August 2022 for those with low (no formal qualification) compared to high (university degree) education, stratified by 10-year age group (from 30 to 89 years). We estimated relative rates using Cox regression, including adjustment for sociodemographic factors.
Results: Among 13.1 million people in our study population, 94% had received a first and 80% a third dose by 31 August 2022. Rates of uptake of first and third dose were around 50% lower for people with low compared to high education. Gaps were small in absolute terms for first dose, and at the end of the study period ranged from 1 to 11 percentage points across age groups. However, gaps were substantial for third dose, particularly at younger ages where the socio-economic gap was as wide as 32 percentage-points.
Conclusion: Education-related inequalities in uptake were larger where discretion in decisions was larger. Policies that limited discretion in decisions to receive vaccines may have contributed to achieving the dual aims of maximising uptake and minimising inequalities.

Introduction

The Australian COVID-19 vaccination program commenced on 22 February 2021 as part of a suite of policies and programs to minimise the impact of COVID-19. Uptake of two doses was among the highest in the world,[1] with over 96% of individuals aged 16 years and over having received at least two doses as of 31 August 2022.[2] In contrast, uptake of a third dose was considerably lower, with approximately 69% of the eligible population having received a third dose by that time.[3]

Third dose vaccination is a crucial component of the national strategy against COVID-19. Compared to people who have received two doses of a COVID-19 vaccine in the previous three months, people who have received a third dose have a significantly reduced risk of infection, hospitalisation and death.[4,5] Understanding how to improve uptake of third and subsequent doses is essential for the long-term success of national vaccination programs, which requires achieving high population coverage with minimal inequalities.[6]

In Australia, third doses were implemented using different policy strategies and in different COVID contexts, and there was more discretion in the decision to receive a third dose compared to first and second doses. As in many other countries, Australia implemented vaccination certificates for the first and second doses.[7] Certificates were issued upon having received two doses. Federal and state level mandated proof of vaccination for a number of employees,[8] and in some states, proof of vaccination was also required for participation in several basic social activities, such as entry into shops and restaurants, and for air travel (see for example).[9] Third doses were not incorporated into vaccine

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certificates, fewer employers required employees to have a third dose as a condition of employment (i.e. only to those providing care services to vulnerable people),[10] and there were no restrictions placed on members of the general public who did not receive a third dose.

At the time the public health advice changed to include a third dose (from November 2021), the Omicron variant was the dominant strain, which was less severe relative to earlier variants.[11] Furthermore, restrictions had eased, borders had reopened and many people had already been infected with the virus. Together, this created a context in which a third dose was viewed as more discretionary than the first and second doses. The effect of discretion on vaccine uptake is unclear, and there are conflicting views on the matter. A number of health professionals have raised concerns about the potential for vaccine certificates to exacerbate social inequalities because of greater vaccine avoidance among those of lower socio-economic position.[12,13] However, others have argued that greater choice in health care-related decisions (e.g. removing vaccine certificates) may exacerbate existing socio-economic inequalities.[14]

The aim of this study was to compare the socio-economic variation in first vs third dose vaccination rates in Australia. We did this to examine whether greater discretion in the decision to receive a vaccination, as was the case in the third compared to the first dose of a COVID-19 vaccine, is associated with widening socio-economic inequalities, to inform future vaccination policy and practice. We did not investigate rates of uptake of a second dose because, as of 31 August 2022, 98% of those who received a first dose had also received a second.[3]

Methods

Data sources

We used linked data from the Multi-Agency Data Integration Project (MADIP). The MADIP is a partnership among Australian government agencies to link administrative and survey data, including data relating to demographic characteristics and health. For this study, we used the following data sources within the MADIP:

1. The Australian Immunisation Register (AIR), which includes a record of all COVID-19 vaccines provided in Australia. Coverage on this register is broader than the Australian population and includes all people on Medicare, as well as people not entitled to Medicare but immunised in Australia by a registered immunisation provider. It also includes a COVID-19 immunisation record for people immunised overseas who have transferred their record to Australia. At the time of writing, approximately 100,000 individuals had opted out of having their immunisation records linked to other administrative data sources and were not included in this analysis. Data from the AIR is currently updated weekly, and for this study, we included vaccines administered up to 31 August 2022.
2. The 2016 Census of Population and Housing, the scope of which was all usual residents of Australia on the night of 9 August 2016 living in private and non-private dwellings. The Census had an estimated person response rate of 94.8%.[15]
3. Death Registrations data, used to exclude people who responded to Census 2016 but who died before the vaccination rollout began and to censor people who died over the course of the vaccine rollout. Death Registrations contain a record of all deaths registered in Australia. For this study, deaths registered in 2016–2021 were available, provisional deaths registered to August 2022 were also available.
4. Overseas migration data, used to exclude those who were not in the country in February 2021 and to censor those who left the country for at least a month as the rollout occurred.

All data as part of the MADIP are linked indirectly using the Person Linkage Spine (see Supplementary material). Linkage rates for each data source to the MADIP Spine are presented in Supplementary Table 1.

Study population

Our study population included those with a Census 2016 record linked to the MADIP Spine, without a linked Death Registration record, who were considered Australian in February 2021 (measured with migration data), and were aged between 30 and 89 years on 22 February 2021. Given that our socio-economic measure is education and that a substantial amount of education formation is still taking place for those aged 25 years and younger, individuals younger than 30 years in January 2021 (i.e. those who were 25 years at Census 2016) were not included in the analysis, despite being eligible for the COVID-19 vaccines. Those aged 90 years and older are included only in supplementary analyses because education is a less sensitive marker of socio-economic position among those at older ages. We excluded people who had missing information on age or sex on the MADIP Spine, as well as those who received their first dose before 22 February 2021. For analyses of the third dose, we also excluded those who received their third dose before 8 November 2021, i.e. before the start of the third dose rollout, a period in which third doses were largely restricted to people who were immunocompromised.

Variables

The outcomes of interest in this study were the first and third doses of a COVID-19 vaccine, ascertained using vaccine type and encounter date within the AIR.

Our measure of socio-economic position was highest level of education, using data from two Census variables: highest level of school completed and highest non-school qualification. Using these two variables, we created five mutually exclusive categories: lowest education level (no post-secondary school qualification and did not complete Year 12); low-intermediate education (no post-secondary school qualification but completed Year 12); intermediate education (other post-secondary school qualification but did not complete Year 12); intermediate to high education (other post-secondary school qualification and completed Year 12); and highest education level (Bachelor's degree or higher, irrespective of whether Year 12 was completed). We focus our inequality estimates on comparing those with the lowest to the highest education level.

Information on age, based on month and year of birth (and estimated as at February 2021), sex, and state of residence as at December 2021, were derived from the combined demographics file as part of MADIP. We also included information on remoteness, country of birth, English language proficiency, care giving status and disability status, grouped into categories as shown in Table 1, measured with Census.

Analysis

In the main analysis, we described proportions of the population by 10-year age group who had received a first and third dose (separately) each week of the rollout (estimated on Sundays, from 28 February 2021). We also described absolute gaps in uptake on 31

Table 1
Characteristics of the study population in relation to highest level of education.

Characteristic	Highest education		Intermediate-high		Intermediate		Low-intermediate		Lowest education		Missing		Total
	n	%	n	%	n	%	n	%	n	%	n	%	
Total	3,478,580	26.5	2,206,910	16.8	2,043,840	15.6	1,629,460	12.4	3,023,730	23.0	735,800	5.6	13,118,330
Age group (years)													
30–39	1,036,010	36.8	656,580	23.3	309,130	11.0	427,050	15.2	288,330	10.2	100,670	3.6	2,817,760
40–49	935,200	34.0	604,950	22.0	351,200	12.8	387,730	14.1	365,570	13.3	103,710	3.8	2,748,350
50–59	666,440	24.6	420,930	15.6	539,250	19.9	318,020	11.8	639,120	23.6	122,290	4.5	2,706,040
60–69	499,780	21.2	299,310	12.7	460,600	19.5	257,880	10.9	705,660	29.9	136,210	5.8	2,359,480
70–79	264,710	15.5	167,090	9.8	282,480	16.5	168,830	9.9	667,110	39.1	157,130	9.2	1,707,350
80–89	76,430	9.8	58,070	7.5	101,190	13.0	69,940	9.0	357,940	45.9	115,800	14.9	779,370
Sex													
Men	1,530,990	24.3	1,128,740	17.9	1,262,500	20.0	766,090	12.1	1,289,340	20.4	329,580	5.2	6,307,250
Women	1,947,600	28.6	1,078,170	15.8	781,340	11.5	863,370	12.7	1,734,390	25.5	406,230	6.0	6,811,100
State													
NSW	1,139,810	27.9	656,490	16.1	644,900	15.8	481,080	11.8	920,790	22.6	236,740	5.8	4,079,810
VIC	958,080	29.2	538,790	16.4	459,510	14.0	412,120	12.6	727,440	22.2	181,630	5.5	3,277,590
QLD	589,610	22.4	481,010	18.2	437,690	16.6	344,610	13.1	641,280	24.3	141,990	5.4	2,636,170
SA	214,890	22.2	157,400	16.3	161,820	16.7	117,470	12.1	263,120	27.2	52,630	5.4	967,350
WA	334,660	24.8	241,000	17.9	218,230	16.2	177,090	13.1	302,610	22.4	74,830	5.5	1,348,410
TAS	62,590	20.6	39,600	13.0	61,120	20.1	28,470	9.4	93,030	30.6	19,050	6.3	303,860
NT	20,710	23.2	15,220	17.0	15,580	17.4	10,310	11.5	21,090	23.6	6450	7.2	89,370
ACT	98,800	45.1	38,410	17.5	19,590	8.9	28,870	13.2	25,190	11.5	8070	3.7	218,940
Other	260	17.8	280	19.2	230	15.8	180	12.3	370	25.3	150	10.3	1460
Missing	59,180	30.3	38,700	19.8	25,160	12.9	29,260	15.0	28,820	14.7	14,270	7.3	195,400
Remoteness													
Major cities	2,850,090	30.7	1,620,310	17.4	1,257,600	13.5	1,235,520	13.3	1,881,540	20.2	453,470	4.9	9,298,520
Inner regional	427,360	17.6	376,970	15.5	516,500	21.3	243,110	10.0	707,910	29.1	156,670	6.5	2,428,510
Outer regional	165,230	14.9	170,420	15.3	223,130	20.1	121,340	10.9	354,380	31.9	76,520	6.9	1,111,020
Rural or remote	32,360	14.1	36,330	15.8	42,500	18.5	27,260	11.9	73,650	32.1	17,390	7.6	229,480
Missing	3540	7.0	2890	5.7	4140	8.1	2220	4.4	6270	12.3	31,750	62.5	50,820
Country of birth													
Australia or New Zealand	2,046,110	23.1	1,492,870	16.8	1,663,640	18.8	1,032,170	11.6	2,195,960	24.8	430,440	4.9	8,861,210
England, Ireland, North America	280,520	28.9	177,680	18.3	153,260	15.8	120,510	12.4	183,870	18.9	55,110	5.7	970,970
Africa	159,240	33.0	98,760	20.5	32,670	6.8	75,210	15.6	91,490	19.0	24,470	5.1	481,850
South East Asia	231,160	38.0	93,170	15.3	29,220	4.8	105,390	17.3	122,940	20.2	26,790	4.4	608,680
North East Asia	230,360	49.8	71,070	15.4	8970	1.9	91,140	19.7	44990	9.7	16,020	3.5	462,550
Southern Central Asia	305,360	56.8	90,380	16.8	14,540	2.7	65,450	12.2	39,630	7.4	22,610	4.2	537,990
South and Central America	41,130	40.5	23,180	22.8	6490	6.4	14,310	14.1	10,440	10.3	6120	6.0	101,660
Europe	134,080	19.3	107,630	15.5	88,500	12.7	78,310	11.3	232,050	33.4	54,310	7.8	694,870
Other Oceania	22,260	21.1	25,120	23.8	9680	9.2	21,040	20.0	20,680	19.6	6610	6.3	105,410
Missing	28,350	9.7	27,050	9.2	36,880	12.6	25,910	8.8	81,670	27.9	93,300	31.8	293,170
English proficiency													
Speaks English well	3,429,380	27.3	2,162,800	17.2	2,019,020	16.1	1,524,800	12.1	2,787,640	22.2	635,230	5.1	12,558,880
Speaks English not well	40,170	9.3	36,920	8.5	17,290	4.0	97,550	22.6	216,610	50.1	23,860	5.5	432,390
Missing	9020	7.1	7190	5.7	7540	5.9	7110	5.6	19,490	15.3	76,730	60.4	127,070
Unpaid adult care giving													
No care giving responsibilities	2,975,620	27.2	1,869,420	17.1	1,693,160	15.5	1,396,140	12.8	2,517,050	23.0	481,880	4.4	10,933,270
Care giver	470,650	26.1	308,930	17.1	316,270	17.5	201,020	11.1	419,560	23.2	90,180	5.0	1,806,590
Missing	32,310	8.5	28,570	7.5	34,420	9.1	32,310	8.5	87,110	23.0	163,740	43.3	378,470
Disability status													
No disability	3,395,110	27.7	2,128,750	17.3	1,930,680	15.7	1,540,690	12.5	2,693,030	21.9	589,280	4.8	12,277,540
Disability	50,340	8.4	52,980	8.9	86,160	14.4	67,990	11.4	284,410	47.5	56,380	9.4	598,270
Missing	33,140	13.7	25,190	10.4	27,000	11.1	20,770	8.6	46,300	19.1	90,150	37.2	242,530

Note: Numbers and proportions are based on numbers that have been randomly perturbed to a number within 10. Education categories: highest education level (Bachelor's degree or higher, irrespective of whether Year 12 was completed); intermediate to high (other post-secondary school qualification and completed Year 12); intermediate education (other post-secondary school qualification but did not complete Year 12); low-intermediate education (no post-secondary school qualification but completed Year 12); lowest education level (no post-secondary school qualification and did not complete Year 12).

August 2022. Age was estimated separately for each week, and we accounted for deaths and outward migration.

We used Cox regression to estimate hazard ratios (HRs, interpreted as rate ratios [RR]) and 95% confidence intervals for uptake of vaccination according to education level, using highest education as the reference category. For analyses of the first dose, the study population was followed from the first day of the National COVID-19 vaccination program (22 February 2021) until they received their first dose, died, left the country or the 31 August 2022 (end of the study period), whichever occurred first.

For models where third dose was the outcome, we additionally restricted the sample to those who had received two doses of a COVID-19 vaccine and were alive and in the country at the time they were first eligible for a third dose. This study population was followed from the date they were first eligible for third dose minus 21 days, until they received their third dose, died, permanently left the country or until 31 August 2022 (end of the study period), whichever occurred first. Day of eligibility was based on date of second dose for third dose and national eligibility rules (see Supplementary file for further information). Eligibility for third dose was bought forward by 21 days to allow for jurisdictional differences in eligibility criteria and to allow for early vaccination.

Cox models were performed separately by 10-year age group (as of February 2021) and were first estimated without adjustment (Model

Table 2
Hazard ratios (and 95% CI) describing inequalities in rates of uptake of first and third dose of a COVID-19 vaccination.

Age group and education level	First dose			Third dose		
	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
30–39 years						
Highest education	1.00	1.00	1.00	1.00	1.00	1.00
High to intermediate	0.63 (0.62–0.63)	0.62 (0.62–0.63)	0.67 (0.67–0.67)	0.60 (0.60–0.60)	0.61 (0.61–0.62)	0.60 (0.60–0.61)
Intermediate	0.50 (0.49–0.50)	0.49 (0.49–0.50)	0.53 (0.52–0.53)	0.45 (0.44–0.45)	0.46 (0.46–0.46)	0.44 (0.44–0.44)
Intermediate to low	0.59 (0.59–0.59)	0.59 (0.59–0.59)	0.62 (0.62–0.63)	0.57 (0.56–0.57)	0.58 (0.58–0.58)	0.57 (0.57–0.57)
Lowest education	0.44 (0.43–0.44)	0.44 (0.43–0.44)	0.45 (0.45–0.46)	0.42 (0.41–0.42)	0.42 (0.42–0.43)	0.40 (0.40–0.41)
Test for trend	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
40–49 years						
Highest education	1.00	1.00	1.00	1.00	1.00	1.00
High to intermediate	0.63 (0.63–0.64)	0.63 (0.63–0.64)	0.67 (0.67–0.67)	0.66 (0.66–0.67)	0.67 (0.66–0.67)	0.67 (0.67–0.67)
Intermediate	0.52 (0.52–0.53)	0.52 (0.52–0.52)	0.55 (0.55–0.55)	0.54 (0.54–0.55)	0.54 (0.54–0.55)	0.54 (0.53–0.54)
Intermediate to low	0.59 (0.58–0.59)	0.58 (0.58–0.59)	0.60 (0.60–0.60)	0.61 (0.60–0.61)	0.60 (0.60–0.61)	0.60 (0.60–0.61)
Lowest education	0.47 (0.47–0.47)	0.46 (0.46–0.46)	0.48 (0.47–0.48)	0.50 (0.49–0.50)	0.49 (0.49–0.49)	0.49 (0.48–0.49)
Test for trend	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
50–59 years						
Highest education	1.00	1.00	1.00	1.00	1.00	1.00
High to intermediate	0.70 (0.70–0.70)	0.70 (0.70–0.70)	0.72 (0.72–0.72)	0.73 (0.73–0.74)	0.74 (0.73–0.74)	0.74 (0.74–0.75)
Intermediate	0.62 (0.62–0.62)	0.62 (0.62–0.62)	0.62 (0.61–0.62)	0.66 (0.65–0.66)	0.66 (0.65–0.66)	0.63 (0.63–0.63)
Intermediate to low	0.64 (0.63–0.64)	0.64 (0.63–0.64)	0.65 (0.64–0.65)	0.67 (0.66–0.67)	0.66 (0.66–0.67)	0.67 (0.67–0.68)
Lowest education	0.55 (0.55–0.55)	0.54 (0.54–0.54)	0.54 (0.54–0.54)	0.59 (0.59–0.6)	0.58 (0.58–0.59)	0.57(0.57–0.58)
Test for trend	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
60–69 years						
Highest education	1.00	1.00	1.00	1.00	1.00	1.00
High to intermediate	0.74 (0.74–0.75)	0.75 (0.74–0.75)	0.77 (0.77–0.78)	0.78 (0.77–0.78)	0.78 (0.78–0.78)	0.79 (0.79–0.80)
Intermediate	0.71 (0.71–0.72)	0.72 (0.71–0.72)	0.70 (0.70–0.71)	0.72 (0.72–0.73)	0.73(0.72–0.73)	0.70 (0.70–0.71)
Intermediate to low	0.67 (0.67–0.68)	0.67 (0.67–0.68)	0.71 (0.70–0.71)	0.69 (0.69–0.69)	0.69 (0.68–0.69)	0.73 (0.72–0.73)
Lowest education	0.64 (0.63–0.64)	0.63 (0.63–0.63)	0.64 (0.63–0.64)	0.65 (0.65–0.66)	0.64 (0.64–0.65)	0.65 (0.65–0.66)
Test for trend	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
70–79 years						
Highest education	1.00	1.00	1.00	1.00	1.00	1.00
High to intermediate	0.80 (0.80–0.81)	0.80 (0.79–0.80)	0.83 (0.82–0.83)	0.81 (0.81–0.82)	0.81 (0.81–0.82)	0.83 (0.82–0.83)
Intermediate	0.81 (0.81–0.81)	0.81 (0.80–0.81)	0.79 (0.79–0.79)	0.78 (0.78–0.79)	0.78 (0.78–0.79)	0.77 (0.76–0.77)
Intermediate to low	0.71 (0.70–0.71)	0.71 (0.70–0.71)	0.75 (0.75–0.76)	0.71 (0.71–0.72)	0.71 (0.71–0.72)	0.75(0.75–0.76)
Lowest education	0.70 (0.70–0.70)	0.70 (0.69–0.70)	0.72 (0.72–0.72)	0.67 (0.67–0.68)	0.67 (0.67–0.67)	0.70 (0.69–0.70)
Test for trend	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
80–89 years						
Highest education	1.00	1.00	1.00	1.00	1.00	1.00
High to intermediate	0.88 (0.87–0.89)	0.87 (0.87–0.88)	0.90 (0.89–0.91)	0.87 (0.86–0.88)	0.87 (0.86–0.88)	0.88 (0.87–0.89)
Intermediate	0.89 (0.88–0.90)	0.89 (0.88–0.90)	0.87 (0.86–0.87)	0.85 (0.84–0.86)	0.84 (0.83–0.85)	0.83 (0.82–0.84)
Intermediate to low	0.75 (0.74–0.76)	0.75 (0.75–0.76)	0.79 (0.79–0.80)	0.76 (0.75–0.77)	0.77 (0.76–0.77)	0.80 (0.79–0.81)
Lowest education	0.72 (0.72–0.73)	0.73 (0.72–0.73)	0.78 (0.77–0.78)	0.71 (0.70–0.71)	0.71 (0.71–0.72)	0.76 (0.75–0.76)
Test for trend	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Notes: Model 1 is unadjusted. Model 2 is adjusted for age (in single years) and sex. Model 3 is further adjusted remoteness, country of birth, English proficiency, care giving status and disability status. Education categories: highest education level (Bachelor's degree or higher, irrespective of whether Year 12 was completed); intermediate to high (other post-secondary school qualification and completed Year 12); intermediate education (other post-secondary school qualification but did not complete Year 12); low-intermediate education (no post-secondary school qualification but completed Year 12); lowest education level (no post-secondary school qualification and did not complete Year 12).

1), then with adjusted for age (single years) and sex (Model 2), and then additionally for state/territory, remoteness, country of birth, English language proficiency, caregiving status and disability (Model 3). Given that not everyone in the study population was eligible for a first dose of the vaccine from the beginning of the rollout, we conducted sensitivity analyses re-estimating HRs for first dose following study participants from the date at which everyone in the age group was eligible under the national rollout. Supplementary analyses examined rates of uptake in relation to education separately for men and women and among people aged 90 years and older. We assessed the proportional hazards assumption with visual inspection of Kaplan–Meier curves and log–log plots.

To reduce risk of disclosure, where absolute numbers of study participants are reported, estimates are based on numbers randomly perturbed to a number within 10.

Analyses were conducted through the ABS virtual DataLab using Stata 15. Ethics approval for this study was granted by the Australian National University Human Research Ethics Committee (reference number: 2022/345). Access to the data was via the ABS Virtual DataLab.

Results

After applying inclusion and exclusion criteria, there were 13.1 million people in the study population (Table 1; flow diagram in Supplementary Fig. 1). By 31 August 2022, 94% of the study population had received a first dose of a COVID-19 vaccine and 80% of those eligible had received a third dose (Supplementary Table 2).

For all age groups, rates of uptake of first and third dose were lower among those who had lower compared to higher levels of education, with absolute and relative inequalities larger among those in the younger and mid- compared to older-age group (Table 2; Figs. 1 and 2). However, the magnitude of the differences, in absolute and relative terms, were substantially larger for third dose compared to first.

For younger- and mid-age cohorts (30–59 years), rates of uptake of the first dose were around 50% lower among those with low compared to high education (HRs in this age group ranged from 0.44 to 0.55; Fig. 1; Table 2 Model 1). Relative rates were similar for the third dose, with rates 50–60% lower among those with low compared to high education (Fig. 2; Table 2 Model 1). For both the

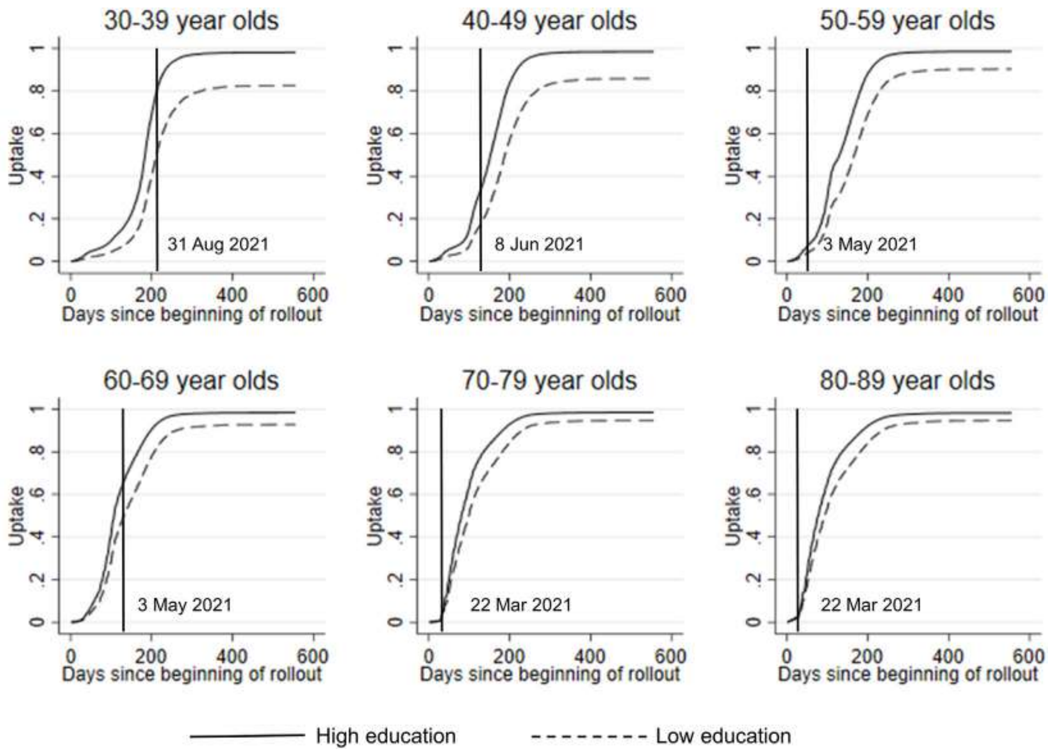

Fig. 1. Crude proportions of the study population who received first dose of a COVID-19 vaccination over time. Notes: Day 0 is 21 February 2021, and the end of the study period (31 August 2022) is day 556. The vertical solid line and the associated date indicate the date at which the age group was eligible for vaccine under the Federal Government rollout program. Low education is defined as those who did not finish school and have no other qualifications. High education is defined as those who have a university qualification. Figures with all education groups plotted are presented in Supplementary Fig. 5.

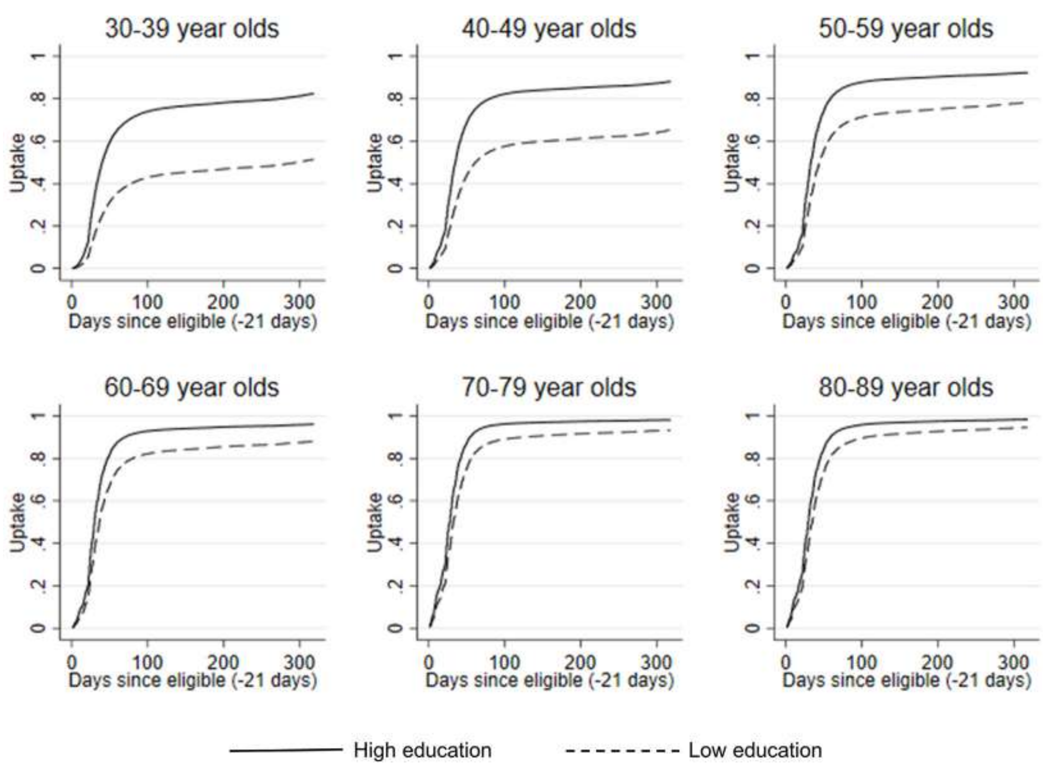

Fig. 2. Crude proportions of the study population who received third dose of a COVID-19 vaccination over time. Notes: Eligibility is based on date of second dose and national rollout rules regarding timing of third dose. Low education is defined as those who did not finish school and have no other qualifications. High education is defined as those who have a university qualification. Figures with all education groups plotted are presented in Supplementary Fig. 5.

first and third doses, RRs were materially unchanged after considering other sociodemographic characteristics (Table 2, Models 2 and 3). Absolute differences in uptake of the first dose were small across all time points of the rollout, and at 31 August 2022, gaps between high and low education ranged from 3.7 percentage points (50–59 years, 92.7% vs 96.4%) to 11 percentage points (30–39 years, 96.4% vs 85.8%) (Table 3). In contrast, education-related gaps in uptake of the third dose were substantial across the rollout, and as of 31 August 2022 ranged from 15 percentage points for those aged 50–59 years (89.2% vs 74.2%) and 32 percentage points for those aged between 30 and 39 years (45.9% vs 78.2%) (Table 3).

Among older adults (60–89 years), uptake of first and third dose was high. Rates were between 36% and 28% lower among those with low compared to high education for first dose and between 35% and 29% lower for third dose (Figs. 1 and 2; Table 2 Model 1), and were materially unchanged after considering other sociodemographic characteristics (Table 2, Models 2 and 3). For both first and third dose among this age group, absolute differences were small (Table 3). For first dose, education-related gaps ranged from 2.2 percentage points (94.3% vs 96.5%) to 1.2 percentage points (95.9% vs 97.1%) for people aged 80–89 years at the end of the study period. For third dose, absolute gaps at 31 August 2022 ranged from 3.3% among those aged 80–89 years (93.3% vs 96.6%) to 8.3% (85.1% vs 93.4%) among those aged 60–69 years.

Relative rates for first dose uptake were similar when the regression analysis was restricted to time periods when all members of the age cohort were eligible under the dates of the national plan (see Supplementary Table 3). Age-specific patterns of results were also not materially different by sex although effect sizes were somewhat larger for men compared to women (Supplementary Figs. 2 and 3; Supplementary Tables 4 and 5). Findings for those aged 90 years and older were similar to those aged 80–89 years (Supplementary Fig. 4; Supplementary Table 6).

Discussion

Using whole-of-population linked data, we found inequalities in rates of uptake of COVID-19 vaccination according to level of education, with absolute differences in uptake considerably larger for third dose compared to first, where there was more discretion in the decision to receive a vaccination. Among older age cohorts, uptake of third dose was high and educational differences were small. However, among the younger and middle age cohorts, low overall uptake of vaccines was, to a large extent, a reflection of much lower uptake among those with low levels of education. Absolute gaps between high and low education in third dose were substantial, being as large as 32 percentage points among those aged 30–39 years, and did not close over the study period.

Socio-economic inequalities in COVID-19 vaccine uptake have been observed in other countries,[16] including England,[17] Israel[18] and Italy.[19] A systematic review of inequalities in COVID-19 vaccination revealed that people of low socio-economic position, including people on low incomes or living in low-income households, were less likely to receive a vaccine.[20] Our finding that uptake was higher overall for doses included on vaccine certificates is also consistent with international evidence.[21,22] To our knowledge, ours is the first study to examine changes in inequalities over time and, in particular, the extent to which inequalities may be exacerbated where there is greater discretion in the choice to be vaccinated. However, one study in the USA among health care workers found that in settings where vaccination was required, uptake of COVID-19 vaccines was higher (90.5% compared to 73.3%) and more equitable across sociodemographic subgroups, including in relation to education level, poverty and insurance status.[23]

Prior to the introduction of COVID-19 vaccination certificates, numerous people raised concerns about their potential to exacerbate existing social inequalities.[7] Our findings show that in the Australian context, there was high overall uptake and smaller education-related inequalities in first dose, the period in which there were vaccination certificates in the decision to be vaccinated, compared to third doses. Decisions to seek out and capacity to access vaccines are complex, reflecting a combination of personal, social and practical factors.[24] Acknowledging that differences in uptake of first and third doses are likely to reflect a number of interacting factors,[24] our findings suggest that policies that reduced discretion in the decision to receive a vaccine (including certificates and mandates) did not exacerbate inequalities in uptake of vaccines and, in fact, may have contributed towards achieving the dual public health aims of increasing overall uptake and minimising socio-economic inequalities.

Our finding that education-related inequalities were larger for third compared to first dose, where there was more discretion and less sense of urgency in receiving a third dose, is consistent with evidence that social inequalities are greater where there is more discretion in health care. There are likely many reasons underpinning this, including socio-economic differences in health literacy and structural barriers affecting ease of access to vaccines. For example, previous research has shown that people of lower SEP are more likely to be concerned about the safety of the vaccine and have a lower perception of personal risk if infected with the virus that causes COVID-19.[25,26]

Policies that limit a person's capacity to make decisions in their health care are generally reserved for personal and public health emergencies. Given this, Australia is unlikely to see the return of

Table 3
Gaps in uptake of vaccines between those with high and low levels of education by 10-year age group, at 31 August 2022.

Age group	First dose			Third dose		
	Highest education	Lowest education	Difference	Highest education	Lowest education	Difference
	%	%	%	%	%	%
30–39 years	96.4	85.8	10.6	78.2	45.9	32.3
40–49 years	96.2	89.4	6.8	83.9	59.6	24.3
50–59 years	96.4	92.7	3.7	89.2	74.2	15.0
60–69 years	96.5	94.3	2.2	93.4	85.1	8.3
70–79 years	96.9	95.7	1.2	96.0	92.1	3.9
80–89 years	97.1	95.9	1.2	96.6	93.3	3.3

Education categories: highest education level (Bachelor's degree or higher, irrespective of whether Year 12 was completed); intermediate to high (other post-secondary school qualification and completed Year 12); intermediate education (other post-secondary school qualification but did not complete Year 12); low-intermediate education (no post-secondary school qualification but completed Year 12); lowest education level (no post-secondary school qualification and did not complete Year 12).

mandated COVID-19 vaccinations for anyone other than those working with the most vulnerable groups. Our findings underscore the importance of understanding the social and structural processes involved in the decision-making process, particularly as there is likely to be greater discretion in decisions regarding COVID-19 vaccines in the future. Strategies addressing socio-economic gradients in barriers to receiving vaccines will be crucial. This includes addressing structural and attitudinal barriers that are more common among relatively disadvantaged populations,[27] and ensuring that communications regarding the risk and benefits of vaccinations (including those beyond the individual) are accessible for all members of the population. These strategies could boost uptake of COVID-19 vaccines further,[25] with the additional benefit of reducing socio-economic inequalities in coverage.

To our knowledge, this is the first study to investigate change in socio-economic inequalities in COVID-19 uptake over time, to examine the extent to which changes are associated with discretion in the choice to be vaccinated. This whole-of-population study used linked administrative data and was able to compare socio-economic inequalities in uptake of the same vaccine over time incorporating different policies and COVID-19 contexts. We had extremely high (>99%) linkage rates between AIR and the MADIP Spine, indicating virtually complete ascertainment of vaccination among the study population, and little evidence of differences in linkage in relation to key sociodemographic characteristics. Using information on Census 2016 allowed us to investigate differences according to education level and the extent to which educational differences were explained by a range of other characteristics. However, these characteristics were measured at least 4 years prior to the start of the rollout, and some characteristics may have changed by the time the rollout began. Use of Census 2016 also necessitated limiting our investigation to adults aged at least 30 years (25 years at the time of Census 2016). We observed relatively low linkage rates to migration data, resulting in likely incomplete removal of people from the study population who left the country before and during the follow-up period and relied on provisional death data for 2022. As a result, some people erroneously included in our study population will appear as though they had not received a vaccination, reducing over rates of uptake. It is unclear to what extent these errors in population scoping are differential with respect to education, and therefore their effect on our inequality estimates is uncertain. Furthermore, we were unable to account for infection with COVID-19, which affects the recommended timing of third dose.[28] Given that infection rates have been higher among people of low socio-economic status,[29] it is likely that we have overestimated inequality in rates of uptake of third dose. However, our finding that gaps persisted past 300 days since first becoming eligible suggests that the inequalities are substantial. Finally, it should be noted that our finding that reduced discretion did not exacerbate existing inequalities based on education does not necessarily extend to people from other marginalised communities.

Conclusion

We observed large differences in uptake of COVID-19 vaccines according to highest level of education, particularly for third dose, where there was greater discretion in uptake. Our findings highlight the importance of structural and social processes for facilitating uptake and indicate potential to optimise uptake further, particularly for younger and middle-aged adults. Given that education-related gaps in uptake of third dose are not closing, additional strategies to address structural and attitudinal barriers will be required to address these gaps.

Author statements

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Data part of the Multi-Agency Data Integration Project are available for approved projects to approved government and non-government users. https://www.abs.gov.au/websitedbs/D3310114.nsf/home/Statistical+Data+Integration+-+MADIP.

Ethical approval

Ethics approval for this study was granted by the Australian National University Human Research Ethics Committee (reference number: 2022/345).

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Competing interests

The authors declare that they have no competing interests.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.puhe.2023.08.020.

References

1. Mathieu E, Ritchie H, Ortiz-Ospina E, Roser M, Hasell J, Appel C, et al. A global database of COVID-19 vaccinations. *Nat Human Behav* 2021;**5**:947–53.
2. Australian Government Department of Health. *COVID-19 vaccination – vaccination data – 31 August 2022*. Canberra, ACT: DOH; 2022.
3. Australian Government Department of Health and Aged Care. *COVID-19 vaccine roll-out*. 9 September 2022. Department of Health and Aged Care; 2022.
4. Mattiuzzi C, Lippi G. Primary COVID-19 vaccine cycle and booster doses efficacy: analysis of Italian nationwide vaccination campaign. *Eur J Public Health* 2022;**32**:328–30.
5. Liu B, Gidding H, Stepien S, Cretikos M, Macartney K. Relative effectiveness of COVID-19 vaccination with 3 compared to 2 doses against SARS-CoV-2 B.1.1.529 (Omicron) among an Australian population with low prior rates of SARS-CoV-2 infection. *Vaccine* 2022;**40**(43):6288–94.
6. Shiri T, Evans M, Talarico CA, Morgan AR, Mussad M, Buck PO, et al. The population-wide risk-benefit profile of extending the primary COVID-19 vaccine course compared with an mRNA booster dose program. *Vaccines* 2022;**10**.
7. Bardosh K, de Figueiredo A, Gur-Arie R, Jamrozik E, Doidge J, Lemmens T, et al. The unintended consequences of COVID-19 vaccine policy: why mandates, passports and restrictions may cause more harm than good. *BMJ Glob Health* 2022;**7**.
8. FairWork Ombudsman. *Orders and directions during coronavirus*. Australian Government; 2022 [7 October 2022]; Available from: https://coronavirus.fairwork.gov.au/coronavirus-and-australian-workplace-laws/tools-and-help-during-coronavirus/other-government-information-and-assistance/list-of-enforceable-government-directions-during-coronavirus.
9. NSW Government. *NSW legislation: public health orders relating to gathering, movement and safety: roadmap for easing restrictions*. Public Health (COVID-19 General) Order 2021. 2021.
10. NSW Government. *NSW legislation: public health orders relating to care services*. Public Health (COVID-19 Care Services) Order 2022. NSW Government; 2022.
11. World Health Organization. *Severity of disease associated with Omicron variant as compared with delta variant in hospitalized patients with suspected or confirmed SARS-CoV-2 infection*. Geneva: World Health Organization; 2022.
12. Voigt K. COVID-19 vaccination passports: are they a threat to equality? *Public Health Ethics* 2022;**15**:51–63.

13. Osama T, Razai MS, Majeed A. Covid-19 vaccine passports: access, equity, and ethics. *BMJ* 2021;**373**:n861.
14. Starfield B, Gérvas J, Mangin D. Clinical care and health disparities. *Annu Rev Public Health* 2012;**33**:89–106.
15. Australian Bureau of Statistics. *Census of population and housing: understanding the census and census data*. Australia: Canberra; 2016. ABS2017.
16. Bergen N, Kirkby K, Fuertes CV, Schlotheuber A, Menning L, Mac Feely S, et al. Global state of education-related inequality in COVID-19 vaccine coverage, structural barriers, vaccine hesitancy, and vaccine refusal: findings from the Global COVID-19 Trends and Impact Survey. *Lancet Glob Health* 2022;**11**: e207–17.
17. Dolby T, Finning K, Baker A, Fowler-Dowd L, Khunti K, Razieh C, et al. Monitoring sociodemographic inequality in COVID-19 vaccination uptake in England: a national linked data study. *J Epidemiol Community Health* 2022;**25**:25.
18. Benderly M, Huppert A, Novikov I, Ziv A, Kalter-Leibovici O. Fighting a pandemic: sociodemographic disparities and coronavirus disease-2019 vaccination gaps-a population study. *Int J Epidemiol* 2022;**51**:709–17.
19. Cesaroni G, Calandrini E, Balducci M, Cappai G, Di Martino M, Sorge C, et al. Educational inequalities in COVID-19 vaccination: a cross-sectional study of the adult population in the Lazio Region, Italy. *Vaccines* 2022;**10**.
20. Bayati M, Noroozi R, Ghanbari-Jahromi M, Jalali FS. Inequality in the distribution of Covid-19 vaccine: a systematic review. *Int J Equity Health* 2022;**21**:122.
21. Walkowiak MP, Walkowiak JB, Walkowiak D. Covid-passport as a factor determining the success of national vaccination campaigns does it work the case of Lithuania vs Poland. *Vaccines* 2021;**9**.
22. Mills MC, Rüttenauer T. The effect of mandatory COVID-19 certificates on vaccine uptake: synthetic-control modelling of six countries. *Lancet Public Health* 2022;**7**:e15–22.
23. Lee JT, Sean Hu S, Zhou T, Bonner KE, Kriss JL, Wilhelm E, et al. Employer requirements and COVID-19 vaccination and attitudes among healthcare personnel in the U.S.: findings from national immunization survey adult COVID module, August – September 2021. *Vaccine* 2022;**40**(51):7476–82.
24. World Health Organization. *Data for action: achieving high uptake of COVID-19 vaccines. Interim guidance*. WHO; 2021.
25. Troiano G, Nardi A. Vaccine hesitancy in the era of COVID-19. *Public Health* 2021;**194**:245–51.
26. Bertoncello C, Ferro A, Fonzo M, Zanovello S, Napoletano G, Russo F, et al. Socioeconomic determinants in vaccine hesitancy and vaccine refusal in Italy. *Vaccines* 2020;**8**:276.
27. Njoku A, Joseph M, Felix R. Changing the narrative: structural barriers and racial and ethnic inequities in COVID-19 vaccination. *Int J Environ Res Public Health* 2021;**18**:9904.
28. Australian Government Department of Health and Aged Care. *COVID-19 booster vaccine advice*. 2022 [12 September 2022]; Available from: https://www.health.gov.au/initiatives-and-programs/covid-19-vaccines/getting-your-vaccination/booster-doses#booster-doses.
29. Khanijahani A, Iezadi S, Gholipour K, Azami-Aghdash S, Naghibi D. A systematic review of racial/ethnic and socioeconomic disparities in COVID-19. *Int J Equity Health* 2021;**20**.

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Original Research

Effect of influenza vaccine subsidies for older adults on vaccination coverage and mortality before and during the COVID-19 pandemic: an ecological study in Japan

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ABSTRACT

Objective: We aimed to determine how municipal subsidies for seasonal influenza vaccines for the elderly affected vaccination coverage and health outcomes and how responses to vaccine prices changed during the COVID-19 pandemic.

Study design and methods: This ecological study includes 1245 municipalities in Japan between 2019 and 2020. Fixed-effects regression analysis was performed to evaluate the effect of influenza vaccine cost subsidy for people aged 65 years or older on vaccination coverage, all-cause mortality, and influenza-related mortality.

Results: The vaccination rate increased when patients' copayments decreased, and reducing the copayment by 1000 Japanese Yen (JPY) was estimated to increase the vaccination rate by 6.3% (95% confidence interval [CI] 4.5—8.2%) in the adjusted model. When examining the additional effect of a zero price compared to a nearly zero price, we found that a zero price increased the immunization rate by 6.4% (95% CI 1.4—11.5%). The effect of copayment on the increase in vaccination coverage was significantly lower during the pandemic than in the pre-pandemic period. The municipal and prefectural analyses found no association between influenza vaccine copayments and all-cause, influenza, or pneumonia mortality.

Conclusion: Cost subsidies and the zero-price effect were shown to increase vaccination coverage but were not associated with relevant mortality measures. Although the impact was attenuated under pandemic conditions, cost subsidy effectively increases the vaccination rate.

In the era of the COVID-19 pandemic, influenza prevention became more critical to avoid concurrent outbreaks of the two diseases. On 21 September 2020, the World Health Organization (WHO) recommended influenza vaccines for high-risk older adults aged 65 years or older during the pandemic.[1] In response to this WHO recommendation, the Japanese government introduced a new policy to emphasize prioritization for influenza vaccination of the elderly in October 2020, just as the third wave of COVID-19 arrived and the influenza season was beginning.[2,3] Since each municipality decided on the actual policy package, some municipalities decided to increase subsidies for influenza vaccination costs or to provide free vaccination in response to the government policy.[4] Consequently, the amount of subsidy varied greatly by municipality.[3]

Vaccine campaigns and improved access to vaccines are known to increase vaccination coverage.[5,6] However, the impact of vaccination costs is mixed. Some studies reported that deductions in vaccination costs were associated with higher vaccination coverage.[7,8] Another study reported that there were heterogeneous effects between urban and rural areas, and lower vaccine prices did not increase national vaccine demand.[9] Furthermore, there is little evidence of the effect of cost subsidies during unprecedented pandemics such as COVID-19. As the willingness to take preventive action may differ during pandemics and non-pandemics, it is essential to examine the effectiveness of influenza vaccine subsidies under COVID-19. In this study, we assessed how municipal subsidies for seasonal influenza vaccines for the elderly affected

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vaccination coverage and health outcomes and how responses to vaccine prices changed during the COVID-19 pandemic.

Methods

Study sample

We conducted the analysis using two administrative units: municipalities and prefectures. This was an ecological study of 1741 municipalities of 47 prefectures in Japan, which have the authority to determine the amount of vaccine cost subsidies. We searched each municipality's website and archived public relation magazines to determine the subsidy amount for vaccines for older adults aged 65 years or older for the 2019/2020 and 2020/2021 influenza seasons. In some municipalities, the exact amount of vaccine copayment was not directly observed because only the information on subsidy was available. In these cases, the estimated vaccine copayment was used as the explanatory variable. The estimated vaccine copayment was calculated by assuming a cost of 3500 yen per vaccination based on the national average price paid for the vaccine without subsidy at medical institutions.[3,10] Although the cost of vaccines may have regional variations, the standard deviation of costs from the survey was 140 yen, suggesting that regional price variations are relatively small.[10] In the prefectural-level analysis, we obtained the weighted average of copayment for vaccination using the number of older adults as the weight.

Measure

This study focused on 2019 and 2020 as the study period. Population data for each prefecture and municipality were as of January 1 of each year.[11] We used the 2019 statistics for each municipality's baseline data (e.g., area and aging rate).[12,13] Data on influenza vaccination rates of each municipality was calculated based on the number of doses from April 1 to March 31 of the following year, which is the fiscal year of Japan's administrative units.[14] Influenza morbidity was monitored at only in 5000 designated sentinel medical facilities in Japan, and data on the epidemic status are provided only by prefecture and are not available for each municipality. Instead, crude mortality and influenza-related mortality were selected as indicators of health outcomes of influenza vaccination. Mortality from influenza and pneumonia were used as influenza-related mortality outcomes. All data on death-related outcomes were derived from Vital Statistics in Japan, which are aggregated and provided from January 1 to December 31 of each year. For the municipality-level analysis, the all-cause mortality rate per 1000 older adults was used as the outcome since data on the causes of death were only available at the prefectural level. For the prefecture-level analysis, mortality per 100,000 people for influenza, pneumonia and all-cause were also calculated. In addition, we calculated the total number of excess deaths in each prefecture from September to the following April to consider excess deaths due to influenza. We tabulated excess mortality based on data generated by the Farrington algorithm that is made available by the National Institute of Infectious Diseases.[15,16] Using the algorithm, the cumulative number of deaths that exceeded or fell short of the estimated number of deaths from September to April of the following year was calculated, and the excess mortality rate per 10,000 population was used as an alternative health outcome.

We also collected data on the number of people infected with COVID-19 as a factor affecting vaccine coverage.[17] Data as of September 1, 2020, were used for the number of COVID-19 cases, as each municipality announces its subsidy for influenza vaccination around September of each year. This study used open data from central and local governments and did not contain personal information; thus, approval by an ethics committee was not required.

Statistical analysis

We conducted analyses using municipality-level data as well as prefecture-level data. As for municipality-level analysis, we analyzed panel data on each municipality's vaccine copayment, vaccination rates, and mortality among older adults. The dependent variables were logarithm-transformed in the analysis; therefore, the estimated value of β approximates the impact in terms of a percent change in the objective variable. The mortality data for older adults contained zeros; therefore, one was added to the data, and a logarithmic transformation was performed. Regression analysis was conducted using a fixed-effects model for each municipality with vaccination rates (%) and the number of deaths per 1000 older adults as dependent variables, as well as vaccine copayment in thousand yen as the explanatory variables. We used four models. The baseline model is expressed by model 1, where Y shows the dependent variable, and Cost shows the copayment of vaccination. The annual fixed effect for 2020 is Y2020; t shows time; and i indicates municipality. The intercept for each municipality (i.e., the municipality fixed effect) is α_i; βs are the coefficients, and ε is the error term.

Model 1.

$$Y_{i,t} = \beta_0 + \beta_1 Cost_{i,t} + \beta_2 Y2020_t + \beta_3 Cost_{i,t} \times Y2020_t + \alpha_i + \varepsilon_{i,t}$$

Model 2 further includes prefecture-specific time trend $\gamma_j t$ to account for differences to control for COVID-19 infection rates and corresponding policies at the prefecture level. j indicates prefecture.

Model 2.

$$Y_{i,t} = \beta_0 + \beta_1 Cost_{i,t} + \beta_2 Y2020_t + \beta_3 Cost_{i,t} \times Y2020_t + \alpha_i + \gamma_j t + \varepsilon_{i,t}$$

A free price is known to have more significance than a price of almost zero. When prices are free, people tend to be loss averse and they do not want to miss the opportunity to get it for free. Thus, offering vaccinations for free (zero price) not only affects demand based on the standard price effect but also introduces an additional influence, leading to an even greater impact on the overall demand for vaccination.[18] Model 3 examines how zero prices affect the outcome: the so-called zero-price effect. The indicator variable that takes unity when vaccine copayment is zero is $1(Cost_{i,t} = 0)$. The coefficient to examine the effect of free vaccination is δ_1. If $\delta_1 > 0$, there is an additional effect of the vaccines' being free.

Model 3.

$$Y_{i,t} = \beta_0 + \beta_1 Cost_{i,t} + \beta_2 Y2020_t + \beta_3 Cost_{i,t} \times Y2020_t + \delta_1 1(Cost_{i,t} = 0) + \delta_2 1(Cost_{i,t} = 0) \times Y2020_t + \alpha_i + \varepsilon_{i,t}$$

Finally, Model 4 is an analogy of Model 2 with zero-price effects.

Model 4.

$$Y_{i,t} = \beta_0 + \beta_1 Cost_{i,t} + \beta_2 Y2020_t + \beta_3 Cost_{i,t} \times Y2020_t + \delta_1 1(Cost_{i,t} = 0) + \delta_2 1(Cost_{i,t} = 0) \times Y2020_t + \alpha_i + \gamma_j t + \varepsilon_{i,t}$$

In addition to the main analysis, we performed single-year cross-sectional analysis for 2019 and 2020, separately.

Some of the outcome variables were available only at the prefecture-level analysis. These outcomes include deaths due to influenza, pneumonia, and excess mortality. For these outcomes as well as vaccination coverage, we performed prefectural analyses by replacing the municipality-level fixed effects with prefecture-level fixed effects. We performed the analysis for vaccination coverage, total deaths, deaths due to influenza, and pneumonia with log-transformation and for excess mortality without log-transformation. All analyses were conducted using RStudio Version 1.4.1717, and $P < 0.05$ was considered statistically significant.

Results

Municipality-level analysis

Of the 1741 surveyed municipalities, 1245 municipalities (71.51%) provided the information about vaccine subsidy in both 2019 and 2020, and these municipalities were analyzed. Vaccine copayments were reduced in 636 municipalities from 2019 to 2020. Comparisons between municipalities with and without reductions in a patient's vaccine copayment are shown in Table 1. The median vaccine copayment decreased from 1500 JPY (Japanese Yen) in 2019 to 500 JPY in 2020. The average national influenza vaccine coverage for older adults significantly increased from 54.89% in 2019 to 67.32% in 2020 ($P < 0.001$). Municipalities with reduced vaccine copayments between the two years had lower aging rates, higher population densities, higher per capita taxable income, lower influenza vaccination rates in 2019, and more COVID-19 infection. Meanwhile, the vaccination rate in 2020 was significantly greater in municipalities with copayment reduction than in those without a change (68.23% vs 66.37%, $P < 0.001$), whereas the vaccination rate in 2019 was the opposite. The number of deaths per 1000 older adults was lower in municipalities with copayment reductions in 2019 and 2020.

Fig. 1a illustrates a linear approximation of the relationship between seasonal influenza vaccination coverage and vaccine copayment among older adults. The fitted line of linear regression of vaccination rates by copayment shows that vaccination rates tend to decline as vaccine copayment increases in both years. Table 2 shows the regression analysis results using fixed-effects models (models 1 and 2) to examine the effects of year and copayment on vaccination rates and mortality. Reducing the copayment by 1000 JPY was estimated to increase the vaccination rate by 8.9% (95% confidence interval [CI] 7.5–10.3%) in the baseline year (i.e., 2019) in the unadjusted model and by 6.3% (95% CI 4.5–8.2%) in the adjusted model, respectively. The coefficient of the interaction term is positive, indicating that the negative correlation between vaccine copayments and vaccination coverage was significantly lower in 2020 than in 2019 and that the effect of copayment decreased during the pandemic. In addition, vaccination rates increased significantly in 2020 from the level in 2019. Similar results were obtained in the single-year analysis (eTable1).

The results of the regression analysis using fixed-effects models that examined the zero-price effect of copayment for the vaccine (models 3 and 4) are shown in Table 2. The adjusted model (model 4) shows that the zero price is associated with a higher vaccination rate for the baseline year. Compared to the near-zero copayment value, the free price is estimated to increase vaccination coverage by 5.1% (95% CI 0.7–9.5%) in the unadjusted model and 6.4% (95% CI 1.4–11.5%) in the adjusted model, respectively. The estimated magnitude of the zero-price effect on the vaccination rate was not significantly different in 2019 and 2020.

Regression analysis, including the effects of each municipality in a fixed-effects model, showed no significant association between vaccine copayment and all-cause mortality for older adults in the baseline year. These findings persisted even after adjusting for prefectural-level effects (Table 3; Fig. 1b).

Compared to the previous year, 2020 had lower deaths per 100,000 persons for influenza and pneumonia but no change in total deaths. Analysis using a fixed-effects model using prefecture-level data also showed that lower copayment for vaccines was associated with higher vaccination coverage (eTable2). However, no association was found between copayment and crude or age-adjusted mortality rates for total mortality, influenza, or pneumonia (Table 4; eFigure 2). There was no association between excess mortality during the influenza season and average copayments on a prefectural level (eTable 4; eFigure 2). Eleven prefectures offered free copayments for seasonal influenza vaccines for persons aged 65 years and older on a prefectural basis (not shown in the table).

Discussion

The influenza vaccination rate among older adults was 12.16% higher in 2020 than in 2019. Regression analysis revealed that the vaccination rate was significantly higher in 2020, indicating that individuals were more willing to get vaccinated as a countermeasure to the COVID-19 pandemic. As previously reported, municipalities had varied reductions in vaccine copayments.[3] Our data showed that low vaccination coverage in 2019 and a high number of COVID-19 cases as of September 2020 were shown as characteristics of municipalities that reduced their vaccine copayment in 2020. These municipalities might have recognized the pandemic threat and implemented promotions to increase vaccination rates, which resulted in lowering copayment. Besides reducing vaccine

Table 1
Comparison of variables between municipalities with and without changes in the copayment between 2019 and 2020.

	Overall	Unchanged	Reduced copayment	*P*-value
N	1245	609	636	
Copayment in 2019 (JPY, median [IQR])	1500.00 [1000.00, 1600.00]	1490.00 [1000.00, 1500.00]	1500.00 [1000.00, 1600.00]	0.002
Copayment in 2020 (JPY, median [IQR])	500.00 [0.00, 1500.00]	1500.00 [1000.00, 1500.00]	0.00 [0.00, 0.00]	<0.001
Aging rate (%, mean (SD))	33.06 (7.13)	33.96 (6.51)	32.21 (7.59)	<0.001
Population (median [IQR])	31475.00 [12345.00, 75843.00]	26410.00 [10889.00, 60029.00]	37424.00 [14538.00, 90912.00]	<0.001
Area (km^2, median [IQR])	110.02 [43.11, 261.31]	144.74 [65.68, 326.50]	76.13 [30.00, 203.06]	<0.001
Population density (/km^2, median [IQR])	260.53 [89.92, 1046.49]	197.24 [71.16, 512.32]	492.72 [113.17, 2110.10]	<0.001
Taxable per capita in 2019 (Thousand JPY, median [IQR])	1238.32 [1060.97, 1440.85]	1189.35 [1046.54, 1356.57]	1297.79 [1078.39, 1522.54]	<0.001
COVID-19 infection rate in Sep/2020 (/100,000, mean (SD))	38.62 (35.57)	26.51 (23.54)	50.22 (40.90)	<0.001
Vaccination rate in 2019 (%, mean (SD))	54.86 (8.03)	56.63 (7.77)	53.16 (7.90)	<0.001
Vaccination rate in 2020 (%, mean (SD))	67.32 (7.29)	66.37 (7.12)	68.23 (7.34)	<0.001
Difference in vaccination rate (%, mean (SD))	12.46 (6.09)	9.74 (4.33)	15.07 (6.38)	<0.001
Mortality of older people in 2019 (/1000, mean (SD))	38.24 (6.95)	38.84 (6.42)	37.67 (7.38)	0.003
Mortality of older people in 2020 (/1000, mean (SD))	36.96 (5.42)	37.30 (5.18)	36.64 (5.62)	0.031

JPY, Japanese Yen; IQR, interquartile range; SD, standard deviation.

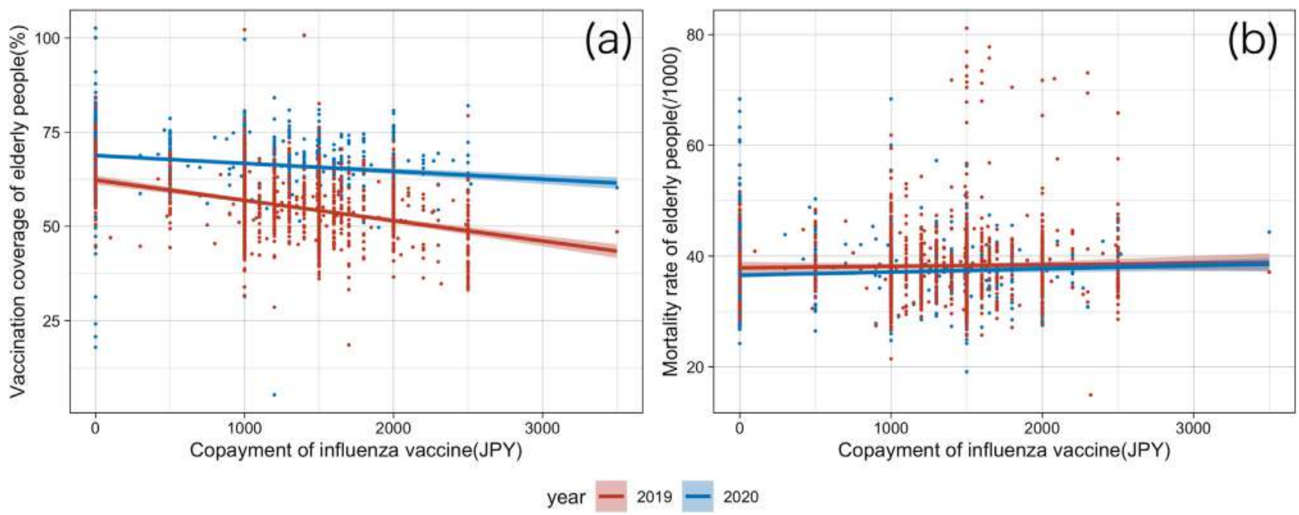

Fig. 1. Relationship between copayments, vaccination rates, and mortality rates at the municipal level. JPY, Japanese Yen.

Table 2
Effects of influenza vaccine copayment on vaccination coverage in municipal-level analysis.

	Unadjusted model		Adjusted model	
	Estimate (95% CI)	*P*-value	Estimate (95% CI)	*P*-value
Models 1 & 2				
Copayment (1000 JPY)	−0.089 (−0.103–0.075)	<0.001	−0.063 (−0.082–0.045)	<0.001
Year dummy	0.135 (0.116–0.155)	<0.001	0.133 (0.081–0.184)	<0.001
Copayment × Year dummy	0.019 (0.005–0.033)	0.009	0.027 (0.010–0.044)	0.002
N	2477		2477	
Adjusted R^2	0.51338		0.54113	
Model 3 & 4 (With zero price effect)				
Copayment (1000 JPY)	−0.072 (−0.091–0.053)	<0.001	−0.043 (−0.068–0.018)	<0.001
Year dummy	0.123 (0.091–0.156)	<0.001	0.086 (0.023–0.149)	<0.001
Zero-price effect	0.051 (0.007–0.095)	0.022	0.064 (0.014–0.115)	0.013
Copayment × Year dummy	0.028 (0.005–0.050)	0.015	0.017 (−0.007–0.041)	0.157
Zero-price effect × Year dummy	−0.011 (−0.058–0.036)	0.649	−0.047 (−0.096–0.002)	0.059
N	2477		2477	
Adjusted R^2	0.51553		0.54278	

CI, confidence interval; JPY, Japanese Yen.

copayments, governments used publicity during the pandemic to increase awareness about health risks. Older adults may have had increased vaccination rates because they believed in the efficacy of vaccines and followed advice from their primary care physicians and government promotions.[19,20] This is consistent with the worldwide trend of increasing influenza vaccine coverage after the start of the COVID-19 pandemic.[21]

This study was conducted using data from Japan, where a universal health insurance program exists. In Japan, irrespective of one's nationality, every resident is automatically enrolled in the national health insurance and long-term care insurance programs.[22] These programs guarantee equal access to medical treatment for all individuals, in principle, with the same copayment requirements. This means that virtually every resident in Japan experiences identical financial burdens when gets infected with influenza. The institutional setting eliminates the influence of differences in healthcare costs for treatment on demand for vaccination, allowing us to examine the pure cost effects of influenza vaccination on vaccine demand.

Previous research showed that copayment influences influenza vaccination coverage, but the magnitude of the effect is not significant.[7,8] In our study, vaccination rates were negatively

Table 3
Effects of influenza vaccine copayment on all-cause mortality among individuals aged 65 years or older in municipal-level analysis.

	Unadjusted model (Model 1)		Adjusted model (Model 2)	
	Estimate (95% CI)	*P*-value	Estimate (95% CI)	*P*-value
All-cause mortality (/1000 older adults)				
Copayment (1000 JPY)	0.007 (−0.008–0.022)	0.395	0.014 (−0.006–0.034)	0.181
Year dummy	−0.013 (−0.034–0.008)	0.222	0.009 (−0.057–0.075)	0.553
Copayment × Year dummy	−0.016(−0.032–0.000)	0.043	−0.023 (−0.042–0.004)	0.018
N	2490		2490	
Adjusted R^2	−0.90485		−0.89348	

CI, confidence interval; JPY, Japanese Yen.

Table 4
Effects of influenza vaccine copayment on mortality due to influenza, pneumonia, and all-cause in prefectural-level analysis.

	Mortality	
	Estimate (95% CI)	*P*-value
Influenza		
Copayment (1000 JPY)	−0.281 (−0.619–0.057)	0.11
Year dummy	−1.616 (−2.121–1.110)	<0.001
Copayment * Year dummy	0.157 (−0.196–0.510)	0.388
N	94	
Adjusted R^2	0.87345	
Pneumonia		
Copayment (1000 JPY)	0.010 (−0.051–0.070)	0.756
Year dummy	−0.187 (−0.278–0.096)	<0.001
Copayment × Year dummy	0.000 (−0.063–0.064)	0.99
N	94	
Adjusted R^2	0.83023	
All-cause death		
Copayment (1000 JPY)	−0.006 (−0.022–0.011)	0.518
Year dummy	−0.014 (−0.039–0.011)	0.284
Copayment × Year dummy	−0.004 (−0.021–0.014)	0.693
N	94	
Adjusted R^2	−0.19406	

CI, confidence interval; JPY, Japanese Yen.

correlated with copayment in a fixed-effects model that considered the variation among municipalities. It was estimated that lowering the copayment for vaccines by 1000 JPY increased the vaccination rate by 6.3%. Assuming the initial vaccination rate of 55%, based on the national average vaccination rate in 2019, a vaccine cost subsidy of 1000 JPY per person would be expected to increase the vaccination rate by 3.47 percentage points. The impact of copayment estimated in this study on vaccination rates was greater than that reported in previous studies.[7,8] Although we have not performed a cost-benefit analysis due to limitations in data availability, previous studies have shown that influenza vaccines for the elderly can save healthcare costs in cost-effectiveness analyses in other countries.[23,24] The results of this study can be utilized by municipalities to develop specific policies on how much they should subsidize the cost to achieve a determined goal for vaccination rates.

Our results showed that copayment amounts had less influence on vaccine coverage in 2020 compared to 2019. The increased public awareness of health risks likely reduced the impact of financial incentives on the decision to vaccinate. Similarly, attitudes toward vaccines changed before and after past influenza pandemics.[8,25,26] Our results are consistent with other studies that show that perceptions of the influenza vaccine have changed since the beginning of COVID-19, and the willingness to be vaccinated has increased.[27,28]

The zero-price effect was originally studied in the field of behavioral economics, and people have a different decision-making reference point when the price is zero, which has an effect beyond the absolute value of the price difference.[18] The zero-price effect has also been studied in the healthcare field, where it has been shown to affect health insurance choices and the behavior around pediatric medical visits.[29,30] The few studies that have been done examining the zero-price effect on vaccinations have not demonstrated its impact.[31,32] This study showed that the magnitude of the zero-price effect on the influenza vaccination rate increase is substantial, estimated to be at 6.4%. This finding seems to suggest that free immunizations would increase coverage compared to a price point of almost free.

The influenza vaccine has reduced influenza, pneumonia, hospitalization, and mortality among older adults.[33,34] However, our study found that vaccine copayments did not change health outcomes in both 2019 and 2020, as measured by the crude mortality rate per 1000 persons aged 65 years and older. Similarly, in the prefectural-level analysis, there was no association between vaccine copayment and influenza, pneumonia, or total mortality. Apart from the increase in vaccine rates, there could be fewer influenza outbreaks and a significant reduction in influenza deaths in 2020 because of the precautious behavior during the COVID-19 pandemic: the use of masks, thorough hand hygiene, and refraining from being around other people.[35] Similar trends have been reported in different countries and for other viral respiratory tract infections.[36–38] Previous systematic reviews of influenza vaccine effectiveness in older adults have demonstrated a reduction in mortality from influenza, pneumonia, and cardiovascular/respiratory disease but no reduction in all-cause mortality; other recent retrospective cohort studies have shown that vaccines reduce all-cause mortality.[39] This demonstrates a discrepancy between the predictions of previous studies examining the efficacy of vaccines and the actual mortality rates obtained from epidemiologic information.[40] There are several possible explanations: First, since all-cause mortality is a nonspecific outcome, it cannot be lowered by the influenza vaccine alone. For example, even if the number of deaths due to the influenza virus may have decreased, the overall mortality rate might not have changed because of the increase in deaths due to COVID-19 in the same municipality. Second, the vaccine only suppresses mortality during the influenza pandemic period and thus has less impact on the annual mortality rate.[40] In this study, mortality data were compiled from January 1 to December 31 of each year, but the influenza epidemic season in Japan is from September to around April of the following year. Therefore, it is possible that the effect of the vaccine subsidy could not be detected because the data do not reflect the period during which the vaccine is effective. Our additional analysis for excess mortality during influenza season also failed to demonstrate the effectiveness of vaccine subsidies. This is because the prefectural-level analyses offset differences in subsidies at the municipal level. Third, RCTs and cohort studies are susceptible to selection bias based on willingness to vaccinate. Therefore, their results could be different from those of studies covering the entire population using mortality statistics, such as this study.

There are several limitations of this study. First, this study was not able to consider the influence of population migration between municipalities in 2019 and 2020. However, demographic data showed that population migration between municipalities was 2.7% lower in 2020 than in 2019, suggesting that the influence of population shift due to the COVID-19 pandemic was relatively small.[41] Second, data on the number of COVID-19 cases and statistics about the cause of death were only available at the prefecture level, not the municipal level, which might have offset differences in cost subsidies for the vaccine in individual municipalities. Third, we only collected data on subsidizing the cost of the vaccination, not other policies to increase vaccination rates, such as improved access to vaccinations, publicity, and changes to the overall healthcare system in response to the COVID-19 pandemic, such as increased numbers of hospital beds. These non-cost policies should be factored in to determine whether cost subsidies are a truly effective and efficient way to increase influenza vaccination rates or reduce influenza mortality.

Conclusion

Vaccination coverage among older adults increased when patients had to provide a lower copayment for influenza vaccines. Furthermore, we observed a zero-price effect, an add-on effect of making the vaccine cost-free. The effect of subsidies was reduced but still significant during the COVID-19 pandemic. We did not find an association between vaccine subsidies and several mortality measures. Our results suggest that vaccination subsidies could be an effective tool to increase vaccination coverage during a pandemic like COVID-19, and making the price zero would potentially produce an additional effect.

Author statements

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Ethical approval

This study used open data from central and local governments and did not contain personal information; thus, approval by an ethics committee was not required.

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Competing interests

All authors declare that they have no conflicts of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.puhe.2023.08.031.

References

1. World Health Organization = Organisation mondiale de la Santé. WHO seasonal influenza vaccination recommendations during the COVID-19 pandemic – recommandations du SAGE de l'OMS pour la vaccination contre la grippe saisonnière pendant la pandémie de COVID-19. *Weekly Epidemiological Record = Relevé épidémiologique hebdomadaire* 2020;**95**(45):539–43.
2. Request for Cooperation for Seasonal Influenza Vaccination Schedule. Ministry of Health, Labor and Welfare. Accessed December 7, 2022. https://www.mhlw.go.jp/stf/seisakunitsuite/bunya/kenkou_iryou/kenkou/kekkaku-kansenshou18/index_00011.html.
3. Ando T, Maruyama T, Tamai A, Murakami T, Kido Y, Ishida T, et al. Disparities in co-payments for influenza vaccine among the elderly, during the COVID-19 pandemic in Japan. *J Infect Chemother* 2022;**28**(7):896–901. https://doi.org/10.1016/j.jiac.2022.03.011.
4. Hirota Y, Kaji M. History of influenza vaccination programs in Japan. *Vaccine* 2008;**26**(50):6451–4. https://doi.org/10.1016/j.vaccine.2008.06.042.
5. Thomas RE, Russell ML, Lorenzetti DL. Systematic review of interventions to increase influenza vaccination rates of those 60 years and older. *Vaccine* 2010;**28**(7):1684–701. https://doi.org/10.1016/j.vaccine.2009.11.067.
6. Blank P, Schwenkglenks M, Szucs TD. The impact of European vaccination policies on seasonal influenza vaccination coverage rates in the elderly. *Hum Vaccines Immunother* 2012;**8**(3):328–35. https://doi.org/10.4161/hv.18629.
7. Ohkusa Y. Policy evaluation for the subsidy for influenza vaccination in elderly. *Vaccine* 2005;**23**(17–18):2256–60. https://doi.org/10.1016/j.vaccine.2005.01.042.
8. Ibuka Y, Bessho S. Subsidies for influenza vaccination, vaccination rates, and health outcomes among the elderly in Japan. *Jpn World Econ* 2015;**36**:56–66. https://doi.org/10.1016/j.japwor.2015.07.001.
9. Kondo M, Hoshi S ling, Okubo I. Does subsidy work? Price elasticity of demand for influenza vaccination among the elderly in Japan. *Health Pol* 2009;**91**(3):269–76. https://doi.org/10.1016/j.healthpol.2008.12.014.
10. Ministry of Health, Labour and Welfare. Survey on unit costs of vaccination contract. Accessed September 2, 2021. https://www.mhlw.go.jp/file/05-Shingikai-10601000-Daijinkanboukouseikagakuka-Kouseikagakuka/0000032800.pdf.
11. Ministry of Internal Affairs and Communications. Surveys of Population, Population Change and the Number of Households based on the Basic Resident Registration. e-Stat; Portal Site of Official Statistics of Japan. Accessed September 8, 2021. https://www.e-stat.go.jp/stat-search/files?page=1&layout=datalist&toukei=00200241&tstat=000001039591&cycle=7&year=20200&month=0&tclass1=000001039601&result_back=1&tclass2val=0.
12. Geospatial Information Authority of Japan. *Technical report of the geospatial information authority of Japan, E2-No.68, the report of statistical reports on the land area by prefectures and municipalities in Japan in*. https://www.gsi.go.jp/KOKUJYOHO/OLD-MENCHO-title.htm, 2020. [Accessed 8 September 2021].
13. Ministry of Internal Affairs and Communications. Survey of taxation of local governments. Accessed September 9, 2021. https://www.soumu.go.jp/main_sosiki/jichi_zeisei/czaisei/czaisei_seido/ichiran09_19.html.
14. Ministry of Health, Labour and Welfare. Report on Regional Public Health Services and Health Promotion Services. Portal Site of Official Statistics of Japan. Accessed September 15, 2022. https://www.e-stat.go.jp/stat-search/files?page=1&toukei=00450025&tstat=000001030884.
15. Kawashima T, Nomura S, Tanoue Y, et al. Excess all-cause deaths during coronavirus disease pandemic, Japan, January–may 2020 - Volume 27, number 3—March 2021 - emerging infectious diseases journal - CDC. doi:10.3201/eid2703.203925.
16. Excess and Exiguous Deaths in Japan | exdeaths-japan.org. Accessed July 13, 2023. https://exdeaths-japan.org/en.
17. Visualizing the data: information on COVID-19 infections. Accessed October 7, 2022. https://covid19.mhlw.go.jp/extensions/public/en/index.html.
18. Shampanier K, Mazar N, Ariely D. Zero as a special price: the true value of free products. *Market Sci* 2007;**26**(6):742–57. https://doi.org/10.1287/mksc.1060.0254.
19. Kajikawa N, Kataoka Y, Goto R, Maeno T, Yokoya S, Ueyamaa S, et al. Factors associated with influenza vaccination in Japanese elderly outpatients. *Infection, Disease & Health* 2019;**24**(4):212–21. https://doi.org/10.1016/j.idh.2019.07.002.
20. Matsui D, Shigeta M, Ozasa K, Kuriyama N, Watanabe I, Watanabe Y. Factors associated with influenza vaccination status of residents of a rural community in Japan. *BMC Publ Health* 2011;**11**:149. https://doi.org/10.1186/1471-2458-11-149.
21. Kong G, Lim NA, Chin YH, Ng YPM, Amin Z. Effect of COVID-19 pandemic on influenza vaccination intention: a meta-analysis and systematic review. *Vaccines* 2022;**10**(4):606. https://doi.org/10.3390/vaccines10040606.
22. Ikegami N, Yoo BK, Hashimoto H, Matsumoto M, Ogata H, Babazono A, et al. Japanese universal health coverage: evolution, achievements, and challenges. *Lancet* 2011;**378**(9796):1106–15. https://doi.org/10.1016/S0140-6736(11)60828-3.
23. Mullooly JP, Bennett MD, Hornbrook MC, Barker WH, Williams WW, Patrocoa PA, et al. Influenza vaccination programs for elderly persons: cost-effectiveness in a health maintenance organization. *Ann Intern Med* 1994;**121**(12):947–52. https://doi.org/10.7326/0003-4819-121-12-199412150-00008.
24. Nichol KL, Margolis KL, Wuorenma J, Von Sternberg T. The efficacy and cost effectiveness of vaccination against influenza among elderly persons living in the community. *N Engl J Med* 1994;**331**(12):778–84. https://doi.org/10.1056/NEJM199409223311206.
25. Peretti-Watel P, Verger P, Raude J, Constant A, Gautier A, Jestin C, et al. Dramatic change in public attitudes towards vaccination during the 2009 influenza A(H1N1) pandemic in France. *Euro Surveill* 2013;**18**(44). https://doi.org/10.2807/1560-7917.ES2013.18.44.20623.
26. Poland GA. The 2009–2010 influenza pandemic: effects on pandemic and seasonal vaccine uptake and lessons learned for seasonal vaccination campaigns. *Vaccine* 2010;**28**:D3–13. https://doi.org/10.1016/j.vaccine.2010.08.024.
27. Domnich A, Grassi R, Fallani E, Spurio A, Bruzzone B, Panatto D, et al. Changes in attitudes and beliefs concerning vaccination and influenza vaccines between the first and second COVID-19 pandemic waves: a longitudinal study. *Vaccines* 2021;**9**(9):1016. https://doi.org/10.3390/vaccines9091016.
28. Domnich A, Cambiaggi M, Vasco A, Maraniello L, Ansaldi F, Baldo V, et al. Attitudes and beliefs on influenza vaccination during the COVID-19 pandemic: results from a representative Italian survey. *Vaccines* 2020;**8**(4):711. https://doi.org/10.3390/vaccines8040711.
29. Iizuka T, Shigeoka H. Is zero a special price? Evidence from child healthcare. *Am Econ J Appl Econ* 2022;**14**(4):381–410. https://doi.org/10.1257/app.20210184.
30. Douven R, van der Heijden R, McGuire T, Schut F. Premium levels and demand response in health insurance: relative thinking and zero-price effects. *J Econ Behav Organ* 2020;**180**:903–23. https://doi.org/10.1016/j.jebo.2019.02.030.
31. Suraratdecha C, Ainsworth M, Tangcharoensathien V, Whittington D. The private demand for an AIDS vaccine in Thailand. *Health Pol* 2005;**71**(3):271–87. https://doi.org/10.1016/j.healthpol.2004.05.005.
32. Cook J, Jeuland M, Maskery B, Lauria D, Sur D, Clemens J, et al. Using private demand studies to calculate socially optimal vaccine subsidies in developing countries. *J Pol Anal Manage* 2009;**28**(1):6–28. https://doi.org/10.1002/pam.20401.
33. Suzuki M, Katsurada N, Le MN, Kaneko N, Yaegashi M, Hosokawa N, et al. Effectiveness of inactivated influenza vaccine against laboratory-confirmed influenza pneumonia among adults aged ≥65 years in Japan. *Vaccine* 2018;**36**(21):2960–7. https://doi.org/10.1016/j.vaccine.2018.04.037.
34. Gross PA, Hermogenes AW, Sacks HS, Lau J, Levandowski RA. The efficacy of influenza vaccine in elderly persons. A meta-analysis and review of the literature. *Ann Intern Med* 1995;**123**(7):518–27. https://doi.org/10.7326/0003-4819-123-7-199510010-00008.

35. Sawakami T, Karako K, Song P. Behavioral changes adopted to constrain COVID-19 in Japan: what are the implications for seasonal influenza prevention and control? *GHM* 2021;**3**(3):125–8. https://doi.org/10.35772/ghm.2021.01066.
36. Cui A, Xie Z, Xu J, Hu K, Zhu R, Li Z, et al. Comparative analysis of the clinical and epidemiological characteristics of human influenza virus vs. human respiratory syncytial virus vs. human metapneumovirus infection in nine provinces of China during 2009-2021. Published online August *J Med Virol* 2022;**18**. https://doi.org/10.1002/jmv.28073. jmv.28073.
37. Shokri A, Moradi G, Moradpour F, Bolbanabad AM, Younsei F, Daftarifard P, et al. Influenza incidence overlapped with COVID-19 or under COVID-19 control measures. *Immunity Inflam & Disease* 2022;**10**(8). https://doi.org/10.1002/iid3.672.
38. Abou El Naja H, Tempia S, Barakat A, Elkholy A, Aman A, Khan W, et al. Influenza activity in the eastern mediterranean region (EMR) in 2020-2021 amidst the COVID-19 pandemic. *BMJ Glob Health* 2022;**7**(Suppl 4):e008506. https://doi.org/10.1136/bmjgh-2022-008506.
39. Lapi F, Marconi E, Gualano MR, Vetrano DL, Grattagliano I, Rossi A, et al. A cohort study on influenza vaccine and all-cause mortality in older adults: methodological concerns and public health implications. *Drugs Aging* 2022;**39**(8):645–56. https://doi.org/10.1007/s40266-022-00958-7.
40. Simonsen L, Taylor RJ, Viboud C, Miller MA, Jackson LA. Mortality benefits of influenza vaccination in elderly people: an ongoing controversy. *Lancet Infect Dis* 2007;**7**(10):658–66. https://doi.org/10.1016/S1473-3099(07)70236-0.
41. Report on Internal Migration in Japan. Portal Site of Official Statistics of Japan. Accessed January 27, 2023. https://www.e-stat.go.jp/en/statistics/00200523.

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Original Research

Enhanced EPIRISK tool for rapid epidemic risk analysis

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ABSTRACT

Objectives: This study aims to create an enhanced EPIRISK tool in order to correctly predict COVID-19 severity in various countries. The original EPIRISK tool was developed in 2018 to predict the epidemic risk and prioritise response. The tool was validated against nine historical outbreaks prior to 2020. However, it rated many high-income countries that had poor performance during the COVID-19 pandemic as having lower epidemic risk.
Study design: This study was designed to modify EPIRISK by reparameterizing risk factors and validate the enhanced tool against different outbreaks, including COVID-19.
Methods: We identified three factors that could be indicators of poor performance witnessed in some high-income countries: leadership, culture and universal health coverage. By adding these parameters to EPIRISK, we created a series of models for the calibration and validation. These were tested against non-COVID outbreaks in nine countries and COVID-19 outbreaks in seven countries to identify the best-fit model. The COVID-19 severity was determined by the global incidence and mortality, which were equally divided into four levels.
Results: The enhanced EPIRISK tool has 17 parameters, including seven disease-related and 10 country-related factors, with an algorithm developed for risk level classification. It correctly predicted the risk levels of COVID-19 for all seven countries and all nine historical outbreaks.
Conclusions: The enhanced EPIRSIK is a multifactorial tool that can be widely used in global infectious disease outbreaks for rapid epidemic risk analysis, assisting first responders, government and public health professionals with early epidemic preparedness and prioritising response to infectious disease outbreaks.

Introduction

The rapid risk analysis tool EPIRISK was initially developed in 2018 as a generic epidemic risk analysis tool, building from an earlier Ebola-specific risk analysis tool.[1] The tool used country-related variables related to sociodemographic factors, geographical factors and health systems, and disease-specific variables such as infectiousness, case fatality rate (CFR) and availability of drugs and vaccines (Supplementary S.Table 1). The EPIRISK tool was developed to calculate the overall risk score for infectious disease outbreaks, using country-related and disease-related parameters to classify the epidemic risk as low, moderate, high and extreme.[2] The tool was validated against historical outbreaks, and results showed that the risk score correlated well with outbreak severity for epidemics prior to 2020.[2]

SARS-COV-2 firstly emerged in China in December 2019[3] and rapidly became a pandemic. As of July 17, 2023, the COVID-19 pandemic has resulted in more than 767.97 million cases and 6.95 million fatalities, with the CFR at 0.90%.[4] In 2020, at the early stage of the pandemic, delayed preparedness and inadequate preventative and control measures were seen in various countries, including the USA and several European countries.[5] Governments and some individuals exhibited resistance towards mask use, social distancing and promoted unproven therapeutics, showing the rise of anti-science attitudes and opposition to certain health practices endorsed by the World Health Organisation (WHO).[6,7]

However, earlier risk analysis models such as the Global Health Security Index (GHSI),[8] which ranked the USA the highest as the most prepared among all countries for pandemic preparedness,[9]

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and the original EPIRISK tool[2] underestimated the severity of COVID-19 in the USA to be 'moderate risk', and therefore failed to predict the high impact of the pandemic in some high-income countries, which actually had poor performance in epidemic response. These tools weighted economic factors highly and overlooked the contribution of dynamic factors based on the contextual situation of countries, such as health inequalities, leadership style of government and national cultural orientation,[10–15] which influence and drive behaviours and decision-making during pandemic situations.

In this study, we aimed to enhance the EPIRISK tool by reparameterizing risk factors and validate the enhanced tool against the COVID-19 risk levels in different countries.

Methods

Basic model

Risk factors and algorithm

The basic model was built on the original EPIRISK tool,[2] and new risk factors were added. The original tool[2] used seven country-related parameters, including income, health expenditure, the state of peace, country's border, physician density, hospital bed density and population density; and seven disease-related parameters, including pathogen, basic reproduction number (R0), mode of transmission, asymptomatic stage, CFR, therapy/drug availability and vaccine availability. We identified three additional country-related risk factors, through analysis of the unfolding pandemic, that appeared to impact COVID-19 disease prevention and control: leadership, cultural orientation and universal health coverage. Thus, in the basic model, a total of 17 risk factors were included (Table 1).

To be consistent with the original EPIRISK,[2] we assigned each parameter with a risk score from 1 to 3 points. Once each risk score was assigned, we took the sum and classified the overall score into four risk levels: low (17.00–25.59 points), moderate (25.60–35.79 points), high (35.80–45.99 points) and extreme (46.00–51.00 points). The cut-off points for each risk level were assigned according to the 50th, 70th and 90th percentiles of the distribution of overall scores.[2]

An initial explanation and algorithm for three new risk factors are provided below.

[1] Leadership

To reduce the risk of epidemics, a country relies on strong national leadership and how the enforcement of public health measures is perceived by the public. This factor is categorised into three levels (strong, medium and weak), and each level is defined according to the leadership style.

① Strong (1 point): Authoritarian/Autocratic (absolute power of the state in the hands of one person or group),[16,17]
② Medium (2 points): Democratic-Pluralist (leader accepts the legitimacy of different societal groups, diversity, democratic institutions),[18]
③ Weak (3 points): Democratic-Populist (leader positions themselves as the only legitimate representative of 'the people', anti-elite rhetoric, denies legitimacy of other parties/leaders)[19] OR Laissez-Faire (French 'allow to do', rejects the practice of government intervention).[20]

In order to assign the overall score for this criterion, two-step algorithms were created (Table 1). Initially, the user's entry of leadership was weighted 50% of the score, and the other 50% was assigned by the Worldwide Governance Indicators (WGI) score,[21] which was classified into three levels: WGI>5 (1 point), $-5<\text{WGI}\leq 5$ (2 points), WGI ≤ -5 (3 points). For the sake of analysis of subjective data entry, three users were selected to input scores of leadership (Supplementary S.Table 2) in order to demonstrate the tool's abilities in this study. We randomly selected one user's score into the basic model. The other two users' entry scores were tested in the final model.

[2] Cultural orientation-based risk

'Cultural orientation-based risk' was defined as the average of risk score across three domains in Hostede's cultural dimensions: individualism, indulgence, long-term orientation.[22] Hofstede identified cultural dimensions based on factor analysis of country averages for value measures.[23] The data were collected from surveys of staff working in different subsidiaries of the same multinational company, IBM, between 1967 and 1973, and updated in 2010.[22,23] The model enabled international comparisons between cultures and has been used before in comparative research.[24] Three of the six domains were selected for inclusion as they had data based on extensive literature review, and there were strong associations between the domains and the risk of infectious disease outbreaks. For countries that did not have cultural dimension values, values were assigned based on countries that had similar geolocation and country-level factors.[25] These values were assigned independently and agreed upon by two researchers, and if discrepancies arose, a consensus was reached after deliberate discussion.

The definitions of the three domains are as follows:

① Individualism is the extent to which individuals prefer to take care of only themselves rather than a wider community.
② Indulgence is the extent to which individuals prefer free gratification of basic and natural human drives.
③ Long-term orientation is the extent to which cultures value past traditions and future reward as opposed to more emphasis on the present.[22,23]

Each domain was assigned a value from 0 to 100 by country. Visual binning of the numerical values allowed for the creation of a categorical variable. Binning of numerical variables introduces non-linearity and tends to improve the performance of the model.[26] Equal-width binning was used to divide the countries according to low risk (lowest third of the values), medium risk (middle third of the values) and high risk (top third of the values). Each risk level was assigned a value from 1 to 3, according to low to high risk, respectively. For each country, the average value of three domains was taken as the overall score for the 'cultural orientation-based risk', which was classified into three levels: low (1 point), medium (2 points) and high (3 points).

[3] Universal health coverage

Universal health coverage is the access to quality essential health services, and safe, effective and affordable medicines and vaccines, without financial hardship - to all who need it, including the most disadvantaged. This indicator from the WHO[27] is an index reported on a unitless scale of 0–100, which was initially divided into three levels: high ($\geq$66.6) = 1 point, medium (33.3–66.6) = 2 points and low ($\leq$33.3) = 3 points.[27]

Evaluation of the basic model

We applied the basic model to nine historical outbreaks in varying low- and high-income countries, which were validated by the original EPIRISK tool.[2] These outbreaks include Hepatitis A

Table 1
The basic model: risk analysis of non-COVID-19 outbreaks for nine countries and COVID-19 for seven countries.

Risk factors	2013 Hepatitis A Italy	2014 Ebola Sierra-Leone	2014 Ebola USA	2015 Zika Brazil	2016 Cholera South Sudan	2017 Diphtheria Bangladesh	2018 Hepatitis A Australia	2018 Measles Japan	2018 Lassa Fever Nigeria	2020 COVID USA	2020 COVID UK	2020 COVID Australia	2020 COVID New Zealand	2020 COVID Vietnam	2020 COVID China	2020 COVID Samoa
Income	1	3	1	2	3	2	1	1	2	1	1	1	1	2	2	2
Health expenditure total (% of GDP)	2	1	1	1	2	3	2	1	3	1	2	2	2	2	2	2
The state of peace	1	1	2	2	3	2	1	1	3	2	1	1	1	1	2	2
Country's border	2	2	2	2	3	2	1	1	2	2	2	1	1	2	2	1
Universal health coverage[a]	1	2	1	1	3	2	1	1	2	1	1	1	1	1	1	2
Physician density (per 1000 people)	1	3	2	2	3	3	1	2	3	1	2	1	1	2	2	3
Hospital bed density (per 1000 people)	2	3	2	2	3	3	2	1	3	2	2	2	2	2	1	3
Population density	3	2	1	1	1	3	1	3	3	1	2	1	1	2	2	1
Leadership[a] *User's entry × 50%*	1	1	1	1.5	0.5	0.5	1	1	1.5	1.5	1	1	1	0.5	0.5	1
WGI × 50%	1	1	0.5	1	1.5	1	0.5	0.5	1.5	0.5	0.5	0.5	0.5	1	1	1
Cultural orientation-based risk[a]	2	2	3	2	2	2	2	2	2	3	3	2	2	1	1	2
Pathogen	3	3	3	3	2	2	3	3	3	3	3	3	3	3	3	3
Basic reproductive number	2	3	3	3	3	3	2	3	3	3	3	3	3	3	3	3
Mode of transmission	2	2	2	1	2	3	2	3	2	3	3	3	3	3	3	3
Asymptomatic stage	3	1	1	3	3	3	3	3	3	3	3	3	3	3	3	3
Case fatality rate	1	3	3	3	3	3	1	3	3	2	2	2	2	2	3	1
Therapy/Drug availability	3	3	3	3	1	1	3	3	3	3	3	3	3	3	3	3
Vaccine availability	2	3	3	3	2	2	2	1	3	2	2	2	2	2	2	2
Risk score	33	39	34.5	36.5	41	40.5	29.5	33.5	46	35	36.5	32.5	32.5	35.5	36.5	38
Risk level	**Moderate**	**High**	**Moderate**	**High**	**High**	**High**	**Moderate**	**Moderate**	**Extreme**	**Moderate**	**High**	**Moderate**	**Moderate**	**Moderate**	**High**	**High**
Expected risk score	**25.6–35.7**	**35.8–45.9**	**25.6–35.7**	**35.8–45.9**	**35.8–45.9**	**35.8–45.9**	**25.6–35.7**	**25.6–35.7**	**46–51**	**35.8–45.9**	**35.8–45.9**	**25.6–35.7**	**25.6–35.7**	**25.6–35.7**	**25.6–35.7**	**25.6–35.7**
Expected risk level	**Moderate**	**High**	**Moderate**	**High**	**High**	**High**	**Moderate**	**Moderate**	**Extreme**	**High**	**High**	**Moderate**	**Moderate**	**Moderate**	**Moderate**	**Moderate**
Matched outcome	√	√	√	√	√	√	√	√	√	**X**	√	√	√	√	**X**	**X**

[a] Three additional risk factors were added on the basis of 14 risk factors from the original EPIRISK tool.

outbreak in Australia (2018), Ebola outbreak in the USA (2014), Measles outbreak in Japan (2018), Diphtheria outbreak in Bangladesh (2017), Zika outbreak in Brazil (2015), Hepatitis A outbreak in Italy (2013), Ebola outbreak in Sierra Leone (2014), Cholera outbreak in South Sudan (2016) and Lassa fever outbreak in Nigeria (2018). The same scores of 14 risk factors from the original EPIRISK study[2] were used in the basic model. We then assigned scores to three new risk factors according to the data sources and algorithm provided in this study (Table 1).

Following the historical outbreaks, we applied the basic model to the COVID-19 outbreaks in different countries. In 2020, a worsening trend of COVID-19 was observed in high-income countries compared to middle-income countries.[28] In order to encompass outbreaks in both high- and middle-income countries[29] and with reported high or low number of cases,[30] we chose four high-income countries,[29] including the UK, USA, Australia and New Zealand, and three middle-income countries,[29] China, Vietnam and Samoa. We collected the epidemiological COVID-19 data of these countries from 1 January 2020 to 31 December 2020, including total reported cases and deaths (CFR calculation), incidence, mortality (Table 2), and the maximum and minimum data of global incidence and mortality.[30] All COVID-19 data were collected from Our World in Data,[30] which collates data from multiple sources, including the WHO, European Center of Disease Control (ECDC), John Hopkins University (JHU) and others. The data were then compared with the official governmental reports from the seven countries for accuracy and consistency.[31–36]

Observed severity levels of COVID-19 in seven countries, 2020

We set the observed severity classifications of the COVID-19 pandemic in seven countries in 2020 based on the incidence and mortality (Table 2). We calculated the ranges of global COVID-19 incidence and mortality,[30] and then we equally divided the ranges into four levels: very high (incidence: 78,041.36–104,054.09 per million population, mortality: 2092.48–2789.92 per million population), high (incidence: 52,028.63–78,041.35 per million population, mortality: 1395.05–2092.47 per million population), medium (incidence: 26,015.91–52,028.62 per million population, mortality: 697.60–1395.04 per million population) and low (incidence: 3.18–26,015.90 per million population, mortality: 0.16–697.59 per million population). In the USA, the incidence (60,536.18 cases per million population) was high, and the mortality (1057.33 cases per million population) was at medium level. Both the incidence (36,597.87 cases per million population) and mortality (1079.39 cases per million population) in the UK were at medium level. The COVID-19 incidence and mortality in the other five countries were at low level.

Expected risk levels of COVID-19 in seven countries in 2020 using EPIRISK

COVID-19, which led to the global pandemic in 2020, was assigned slightly higher severity levels in the basic model than diseases such as hepatitis A, cholera and measles, which caused less widespread outbreaks. Therefore, we set the expected severity of COVID-19 in the UK and USA as high, and that in Vietnam, China, Australia, New Zealand and Samoa as moderate, due to known outcomes of the disease in 2020 in these countries (Table 1).

Disease-related risk factors rationale for COVID-19

Details of all disease-related risk factors and scoring from the original EPIRISK framework were described previously.[2] For COVID-19, the following rationales were used for the scores. COVID-19 is the disease caused by the SARS-CoV-2 virus (pathogen: 3 points). The airborne transmission was documented (mode of transmission: 3 points).[37] People infected with SARS-CoV-2 could be asymptomatic (asymptomatic stage: 3 points), or experience mild to severe illness, and even death. The R0 of the dominant strain in early 2020 (D614G) ranged from 0.4 to 4.6 (median: 2.5) (3 points).[38] The calculated country-specific CFR in 2020 was 1.75% in the USA (2 points), 2.95% in the UK (2 points), 3.20% in Australia (2 points), 1.16% in New Zealand (2 points), 5.32% in China (3 points), 2.39% in Vietnam (2 points) and 0.00% in Samoa (1 point) (Table 2).[39] Several vaccines to prevent or reduce the severity of SARS-CoV-2 infection were approved for use in 2020 (1 point), but no effective therapy and drugs were approved until 2021 (3 points).[40]

Country-related risk factors rationale for COVID-19

For the three new risk factors (leadership, cultural orientation-based risk and universal health coverage), we provided the scores (Table 1) with data (Table 3) based on the initial algorithm described in this study. For the other seven factors that were described previously in the original EPIRISK tool[2] (Supplementary S.Table 1), we collected the latest available data as of December 31 in 2020 from the World Bank[29] and the Institute for Economics and Peace[41] (Table 3), and updated scores in the basic model (Table 1).

Risk classification by the basic model

In the basic model (Table 1), we compared the assessed risk levels with the expected risk levels to see the matched and unmatched outcome. The basic model correctly classified the risk levels of all the nine historical outbreaks and the COVID-19 severity in the UK, Vietnam, Australia and New Zealand. However, it failed to classify the risk levels of COVID-19 in the USA, China and Samoa.

Calibration

Based on the basic model, three steps were involved in the calibration process, in order: (i) for the leadership criterion, we adjusted the proportion of the user's entry from 0% to 100% of the score to examine the results; (ii) given there were 10 country-related parameters and seven disease-related parameters, we set 70% of the country-based parameters' overall score to see if the equal contribution could improve the correct rate; (iii) we changed the cut-off points of risk factors to reclassify three scoring levels. A series of models were created during the three steps above, until we found the best-fitting model that could retain the correct risk

Table 2
COVID-19 case and death numbers and rates of incidence, mortality and case fatality in seven countries (1 January 2020 to 31 December 2020).

Country	Cases	Deaths	Incidence (per million population)	Mortality (per million population)	Case fatality rate
USA	20,153,407	352,001	60,536.180	1057.330	1.75%
UK	2,496,235	73,622	36,597.869	1079.389	2.95%
Australia	28,425	909	1102.248	35.249	3.20%
New Zealand	2162	25	444.797	5.143	1.16%
Vietnam	1465	35	14.923	0.357	2.39%
China	87,117	4634	60.321	3.209	5.32%
Samoa	2	0	9.993	0.000	0.00%

Source: Data on COVID-19 (coronavirus) by Our World in Data.[30]

Table 3
Data on country-related risk factors for COVID-19 in seven countries.

Risk factors		USA	UK	Australia	New Zealand	Vietnam	China	Samoa
Income		High	High	High	High	Middle	Middle	Middle
Health expenditure total (% of GDP)		16.77	10.15	9.91	9.74	5.25	5.35	6.36
The state of peace		Low	High	High	High	Medium	Medium	High
Country's border		Land and maritime	Land and maritime	All maritime	All maritime	Land and maritime	Land and maritime	All maritime
Universal health coverage[a]		82.60933	87.71524	87.15386	85.53363	69.54382	82.16772	53.44973
Population density		36	278	3	19	314	150	70
Physician density (per 1000 populations)		2.6	5.8	3.3	3.4	0.8	2	0.3
Hospital bed density (per 1000 populations)		2.9	2.5	3.8	2.6	2.6	4.3	1
Leadership[a]	User's entry	Weak	Medium	Medium	Medium	Strong	Strong	Medium
	WGI	Medium	Medium	Medium	Medium	Strong	Strong	Medium
Cultural orientation-based risk[a]		High	High	Medium	Medium	Low	Low	Medium

Data sources: World Bank[29] and the Institute for Economics and Peace.[41]
[a] Three additional risk factors were added on the basis of seven country-based risk factors from the original EPIRISK tool.

classifications of nine historical outbreaks and be able to correctly classify the risk levels of COVID-19 in all seven countries. The other two users' scores on 'leadership' were tested in the best-fitting model.

Kendall correlation was used to measure the degree of agreement between the levelled incidence, mortality and the predicted risk levels of COVID-19.

Results

A total of 21 models were created to test the risk levels of historical non-COVID outbreaks in nine countries and COVID-19 in seven countries in 2020. After adjusting the cut-off points of 'The state of peace' and 'Universal health coverage', there were two models (Table 4, Supplementary S.Table 3) showing all risk levels matched with the expected risk levels, indicating both models correctly classified risk levels for all outbreaks. The best-fitting model (Table 4), in which the 'leadership' was scored without WGI data, was considered as the final EPIRISK algorithm (Table 5). Even though the 'leadership' was assigned with different scores by three users, this best-fitting model still achieved the 'matched outcome' for all outbreaks' risk levels. The Kendall correlation between incidence and risk level was 0.70, and the correlation between mortality and risk level was 0.73. Both showed a clear positive correlation, which supported the consistence between the observed and predicted COVID-19 severity level by the best-fitting model.

For the enhanced EPIRISK tool, the overall score ranges from 17 to 51 points. To be consistent with the original EPIRISK tool,[2] the cut-off points of risk levels were still set at the 50th, 70th and 90th percentiles of the distribution of the overall score: extreme (46.00–51.00 points) – immediate action required, high (35.80–45.99 points) – action plan required, medium (25.60–35.79 points) – specific monitoring required and low (17.00–25.59 points) – routine procedure.

Discussion

The enhanced EPIRISK tool shows improved risk analysis with validation against the COVID-19 pandemic for seven countries. The risk classification by the enhanced EPIRISK tool correlates well with the COVID-19 severity level based on the observed incidence and mortality rates, indicating that the influence of leadership, culture and universal healthcare should be included in any risk analysis tool. Traditional tools rely more heavily on socio-economic factors such as GDP.[49] The enhanced EPIRISK tool also retained the correct risk classifications of nine non-COVID outbreaks.

The accuracy of risk analysis tools in predicting outbreaks depends on parameters included and data input.[50,51] Evaluation of such tools could be done by validation against retrospective outbreaks or prospectively in real-time outbreaks.[52] Tools such as the GHSI[11] and the Epidemic Preparedness Index (EPI) have been developed to assist governments in improving preparedness for infectious disease outbreaks.[53] However, the failure of these tools, including the original EPIRISK tool, to predict poor outcomes of the COVID-19 pandemic in high-income countries[7,9–11,54] using biological, demographic and socio-economic indices, highlights the need for consideration of additional factors such as culture, leadership and universal healthcare coverage.[15,55]The scores published by the GHSI in October 2019, just before the COVID-19 pandemic was declared, indicated that the USA and UK were the most prepared for a pandemic.[54] However, both countries did not fare well in their response to COVID-19.[9,56] Similarly, the EPI scores released in 2019, which ranked countries according to five levels of preparedness, placed the USA and UK in the higher categories.[7,53] This can be attributed to the lack of consideration of the contribution of leadership, culture and universal healthcare, all of which determine or motivate behaviours, choices and outcomes during pandemics. These are dynamic factors that can change with the contextual situation of countries. Even though the GHSI measured trust in government, it neglected the role of political leadership and ideology in shaping public health responses.[7] For example, the GHSI ranked New Zealand lower than the USA and UK, but the effective and clear communication by the Arden administration in New Zealand may have contributed to comparatively better pandemic outcomes, such as the lower CFR (1.16%) of COVID-19 in New Zealand compared to that in the USA (1.75%) and UK (2.95%) in 2020.[8,57] In contrast, in the USA and UK, governments failed to accept scientific evidence and promoted unproven interventions ranging from 'herd immunity' from infection to unproven drugs, even opposing the WHO in some instances.[6,7] During the first year of COVID-19, countries like Vietnam, Australia, New Zealand and Samoa fared better than the USA or UK through use of measures such as border closure and strict public health measures, which were more culturally acceptable in these countries. In Australia, the government showed leadership by declaring the pandemic on 21 January 2020 prior to the announcement by the WHO.[58] Universal health coverage is also an important determinant of risk, with poorer health outcomes in countries without this.[59] Additionally, it has been well documented that cultural differences at the national or individual level account for differences in risk perceptions and health behaviours.[60] Public health measures are draconian by nature, requiring measures that reduce contact between people or require intervention, such as masks, to reduce the transmission of contagious infections. This is less palatable in highly individualistic cultures compared to more collective cultures. Understanding the cultural values of a society, including individualism vs. collective values, would guide policymakers to frame and implement

Table 4
The best-fitting model: risk analysis of non-COVID-19 outbreaks for nine countries and COVID-19 for seven countries.

Risk factors	2013 Hepatitis A Italy	2014 Ebola Sierra-Leone	2014 Ebola USA	2015 Zika Brazil	2016 Cholera South Sudan	2017 Diphtheria Bangladesh	2018 Hepatitis A Australia	2018 Measles Japan	2018 Lassa Fever Nigeria	2020 COVID USA	2020 COVID UK	2020 COVID Australia	2020 COVID New Zealand	2020 COVID Vietnam	2020 COVID China	2020 COVID Samoa
Income	1	3	1	2	3	2	1	1	2	1	1	1	1	2	2	2
Health expenditure total (% of GDP)	2	1	1	1	2	3	2	1	3	1	2	2	2	2	2	2
The state of peace	1	1	2	2	3	2	1	1	3	3	1	1	1	2	2	1
Country's border	2	2	2	2	3	2	1	1	2	2	2	1	1	2	2	1
Universal health coverage[a]	1	2	1	1	3	2	1	1	2	1	1	1	1	1	1	1
Physician density (per 1000 people)	1	3	2	2	3	3	1	2	3	1	2	1	1	2	2	3
Hospital bed density (per 1000 people)	2	3	2	2	3	3	2	1	3	2	2	2	2	2	1	3
Population density	3	2	1	1	1	3	1	3	3	1	2	1	1	2	2	1
Leadership[a]	2	3	2	3	3	1	2	2	3	3	2	2	2	1	1	2
Cultural orientation-based risk[a]	2	2	3	2	2	2	2	2	2	3	3	2	2	1	1	2
Pathogen	3	3	3	3	2	2	3	3	3	3	3	3	3	3	3	3
Basic reproductive number	2	3	3	3	3	3	2	3	3	3	3	3	3	3	3	3
Mode of transmission	2	2	2	1	2	3	2	3	2	3	3	3	3	3	3	3
Asymptomatic stage	3	1	1	3	3	3	3	3	3	3	3	3	3	3	3	3
Case fatality rate	1	3	3	3	3	3	1	3	3	2	2	2	2	2	3	1
Therapy/Drug availability	3	3	3	3	1	1	3	3	3	3	3	3	3	3	3	3
Vaccine availability	1	3	3	3	1	1	1	1	3	1	1	1	1	1	1	1
Risk score	**32**	**40**	**35**	**37**	**41**	**39**	**29**	**34**	**46**	**36**	**36**	**32**	**32**	**35**	**35**	**35**
Risk level	**Moderate**	**High**	**Moderate**	**High**	**High**	**High**	**Moderate**	**Moderate**	**Extreme**	**High**	**High**	**Moderate**	**Moderate**	**Moderate**	**Moderate**	**Moderate**
Expected risk score	**25.6–35.7**	**35.8–45.9**	**25.6–35.7**	**35.8–45.9**	**35.8–45.9**	**35.8–45.9**	**25.6–35.7**	**25.6–35.7**	**46–51**	**35.8–45.9**	**35.8–45.9**	**25.6–35.7**	**25.6–35.7**	**25.6–35.7**	**25.6–35.7**	**25.6–35.7**
Expected risk level	**Moderate**	**High**	**Moderate**	**High**	**High**	**High**	**Moderate**	**Moderate**	**Extreme**	**High**	**High**	**Moderate**	**Moderate**	**Moderate**	**Moderate**	**Moderate**
Matched outcome	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	**X**

[a] Three additional risk factors were added on the basis of 14 risk factors from the original EPIRISK tool.

Table 5
The enhanced EPIRISK scoring criteria.

ID	Risk Factors	Risk scores			Explanation
		1 point	2 points	3 points	
1	Pathogen	Others	Bacterial	Viral	The type of disease pathogen has an association with the disease spreading. Viral pathogen is likely to cause widespread epidemic because of its extensive growth in a relatively short period of time. Thus, infectious disease by viral pathogen can spread faster than any other pathogen.
2	Basic reproductive number	<1	1–2	>2	The basic reproductive number is the number of secondary infections produced by the index patient. The bigger the basic reproductive number, the higher it is to become an epidemic and the harder to control that epidemic.
3	Mode of transmission	Vector borne/ Zoonosis	Foodborne/ Waterborne/Direct Contact/Bodily fluids/ Bloodborne/Fecal-oral route	Airborne/Droplet	Different modes of transmission will affect the spread of the infectious disease in the community. The disease that spreads via airborne/droplet has a higher risk of widespread outbreak than the disease that spreads through animal or vector.
4	Asymptomatic stage	No		Yes	The disease with a stage has a higher risk of epidemic. The asymptomatic patient contributes to the disease transmission; however, this patient is likely to miss from the detection. It makes the disease spreading go even harder to control.
5	Case fatality rate	<1%	1%–5%	>5%	Potential impact on mortality of the disease can be used as an essential indicator in risk prediction. The highest of range is used to categorise risk scores.
6	Therapy/Drug availability	Yes		No	The spread of a disease will be increasingly difficult to control if there is no definitive therapy available for the disease. With definitive therapy, the spread of the disease can be minimised by reducing the natural duration of the disease. Additionally, the presence of definitive therapy will reduce the severity of the disease outcome.
7	Vaccine availability	Yes		No	Vaccines provide immunity to the disease, particularly for the susceptible population. Implementation of the vaccination program is a very effective control measure to reduce the risk of disease outbreaks. With the availability of the vaccines, the process of infectious disease spreading can be minimised. The best outcome of vaccine availability would be attained if the vaccine is broadly given to all populations in a country through the National Immunisation Program (NIP). However, the list of available vaccines in NIP is different from one country to the other. Only vaccines included in Expanded Immunisation Program (EPI) would be available in every country NIP.
8	Income	High-income country	Middle-income country	Low-income country	The country's capacity in outbreak control is strongly associated with the total GDP. The World Bank divides countries into three categories: high-, middle- (upper and lower) and low-income countries based on their total GDP.[42]
9	Health expenditure Total (% of GDP)	Upper third (>10.0%)	Middle third (5.0 –10.0%)	Lower third (<5.0%)	Health expenditure indicates the proportion of country GDP that assigned to the health sector expenditure. The proportion of health expenditure in a country has a strong association with the healthcare service provided to the population. Country's health expenditure spread was divided into upper, middle and lower third.[43]
10	The state of peace	High peace	Middle peace	Low peace	The states of peace correlate to the country's health system. In a conflict-affected country, access to essential service is poor. As a consequence, population in that country become more vulnerable to the infectious disease transmission. In addition to detection, containment and control of the outbreak are huge challenges in the conflict-affected populations. According to the Global Peace Index rankings provided by the Institute of Economic and Peace, this framework categories the state of peace into three different groups: high (ranking <55), medium (ranking 55–108) and low peace (ranking >108).[41]
11	Country's border	Maritime only	Mixed maritime-land	Land only	The country border is associated with the mobility, accessibility of transportation mode as well as time required to travel. Land border has higher likelihood of interborder disease transmission than water border because of its easiest access for people migration, including those affected by the disease.[44]
12	Population density	<100	100–1000	>1000	Overcrowding is one of the major factors in the disease transmission risk which lead to an epidemic event. Epidemics of disease occur more frequently and severely in a high-density population than in low-density population.[45]
13	Physician density (per 1000)	>2.9	0.8–2.9	<0.8	Adequate size and skill of physician is critical for a country to attain population health goal through provision of sufficient basic medical care. Lack of availability and accessibility to the physician service could aggravate the impact of an outbreak because of delayed in medical treatment. The WHO report indicates the range of physician-weight population density per 1000 population: <0.8 as low, 0.8–2.9 as middle and >2.9 as high.[46]
14	Hospital bed density (per 1000)	>4	2–4	<2	Hospital beds is an indicator for available resources to deliver healthcare service. Without sufficient hospital beds, especially during outbreak event, the likelihood of worse impact increases. Especially when insufficient resources force patients to stay longer in community, which will increase the risk of disease transmission in the community.[47]
15	Leadership	Strong	Medium	Weak	To reduce the risk of epidemics, a country relies on strong national leadership and how enforcement of measures is perceived by the public. This risk factor is categorised into three levels (strong, semi-strong and weak), and each level is defined according to the leadership style.

(*continued on next page*)

Table 5 (*continued*)

ID	Risk Factors	Risk scores			Explanation
		1 point	2 points	3 points	
					①Strong (1 point): Authoritarian/Autocratic (absolute power of the state in the hands of one person or group),[16,17] ②Medium (2 points): Democratic-Pluralist (leader accepts the legitimacy of different societal groups, diversity, democratic institutions),[18] ③Weak (3 points): Democratic-Populist (leader positions themselves as the only legitimate representative of 'the people', anti-elite rhetoric, denies legitimacy of other parties/leaders)[19,48]; OR Laissez-Faire (French 'allow to do', rejects the practice of government intervention).[20]
16	Cultural orientation-based risk	Low	Medium	High	Average of risk score of three domains in Hosteds's cultural dimensions: individualism, indulgence, long-term orientation.[22,23] Details on each domain are presented in 16a,b and c.
16a	*Individualism*	*Collective*	*Moderately individualistic*	*Highly individualistic*	*Individualism describes societies where 'the ties between individuals are loose,' whereas collectivism describes societies where individuals are 'integrated into strong, cohesive in-groups'. Individualism (vs collectivism) is the extent to which individuals prefer to take care of only themselves rather than a wider community. This scale reflects the position of a national culture on a bipolar continuum based on Hofstede's cultural dimensions.*
16b	*Indulgence*	*Restrained*	*Moderately indulgent*	*Highly indulgent*	*The dimensions of indulgence and restraint were later added to the Hofstede model and reflects how a culture responds to basic human needs. This dimension describes the tendency within a society to allow gratification of human desires and impulses related to enjoying life and having fun. High indulgence cultures tend 'to allow relatively free gratification of basic and natural human desires related to enjoying life and having fun,' while for restraint cultures, 'such gratifications needs to be curbed and regulated by strict social norms'.* *Indulgent cultures or individuals typically experience greater happiness, enjoy more freedom, personal choice, and control over their life compared to more restrained cultures.*
16c	*Long-term orientation*	*Highly long-term oriented*	*Moderately long-term oriented*	*Short-term oriented*	*Long-term orientation measures the degree to which people plan for the future rather than today based on Hofstede's cultural dimensions. Additionally, individuals who generally think and act in a future-oriented manner will find it more acceptable to delay gratifications. Cultures with long-term orientation value past traditions and future rewards, as well as related virtues such as perseverance and thrift. However, cultures with short-term orientation put more emphasis on the present.*
17	Universal health coverage	High	Medium	Low	Universal health coverage is access to quality essential health services, and safe, effective and affordable medicines and vaccines, without financial hardship – to all who need it, including the most disadvantaged. This indicator from the WHO is an index reported on a unitless scale of 0–100, which was divided into three levels: high (>50), medium (33–50) and low (<33).[27]

mitigation measures in a way that would gain the cooperation of individuals to comply.[61] Therefore, based on lessons learned from the COVID-19 experience, the enhanced EPIRISK tool considered leadership, cultural orientation and universal health coverage to provide a more predictive risk analysis.

The main limitation of this study is that the small sample of countries we selected for the calibration and validation might not fully represent the variations of the COVID-19 impact between all countries. Although we validated against COVID-19 in seven countries and historical non-COVID outbreaks in nine countries, there is uncertainty in applying the model to COVID-19 outbreaks in other countries. The model could be improved with a wider range of data from all countries using a machine learning approach for calibration and validation in future, aiming to find the best-fitting model based on a larger training data set.[62] This is the work we are undertaking. Another limitation is the COVID-19 data bias. COVID-19 data in 2020 has been updated frequently since it was released, perhaps because the number of cases and deaths was overestimated or underestimated previously, and there may have been delays in outcome data reporting and inclusion in publicly available data sets.[30] In order to minimise data bias, we used the COVID-19 data provided by Our World in Data,[30] which collected data from multiple validated sources. Additionally, the current EPIRISK tool requires users to assign risk scores and calculate the result manually, which introduces some subjectivity. Subjectivity in the selection of the new variables and the assignment of the values to variables are a further limitation. In conclusion, the enhanced EPIRISK tool can rapidly prioritise epidemic response for global infectious disease outbreaks with improved predictive power. In addition to the standard approach of using disease- and country-specific social, demographic and economic factors, we showed that accounting for leadership, culture and universal healthcare may explain the failure of previous tools to correctly predict the performance of countries during COVID-19. We are developing an automated EPIRISK tool on web and mobile applications with real-time data retrieved from live data sources. Use of comprehensive tools like EPIRISK will assist health agencies and public health professionals with rapid risk prediction and more effective epidemic response.

Author statements

Ethical approval

Not applicable, as no animals or human participants, nor identifying data were involved in this study.

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Competing interests

All authors stated that there are no competing interests to declare for the study.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.puhe.2023.08.032.

References

1. Ajisegiri WS, Chughtai AA, MacIntyre CR. A risk analysis approach to prioritizing epidemics: Ebola virus disease in West Africa as a case study. *Risk Anal* 2018;**38**(3):429–41.
2. Lesmanawati DA, Veenstra P, Moa A, Adam DC, MacIntyre CR. A rapid risk analysis tool to prioritise response to infectious disease outbreaks. *BMJ Glob Health* 2020;**5**(6):e002327.
3. World Health Organisation. *Novel coronavirus – China*. 2020. https://www.who.int/csr/don/12-january-2020-novel-coronavirus-china/en/. [Accessed 30 January 2020].
4. Our World in Data. Cumulative confirmed COVID-19 cases and deaths, world. https://ourworldindata.org/grapher/cumulative-deaths-and-cases-covid-19. Accessed October 15, 2021.
5. Hale T, Angrist N, Goldszmidt R, Kira B, Petherick A, Phillips T, et al. A global panel database of pandemic policies (Oxford COVID-19 Government Response Tracker). *Nat Human Behav* 2021;**5**(4):529–38.
6. Bosancianu CM, Dionne KY, Hilbig H, Humphreys M, Sampada K, Lieber N, et al. *Political and social correlates of Covid-19 mortality*. 2020.
7. Baum F, Freeman T, Musolino C, Abramovitz M, De Ceukelaire W, Flavel J, et al. Explaining covid-19 performance: what factors might predict national responses? *BMJ* 2021:372.
8. Baskin J. *COVID-19 and the Global Health Security Index (GHSI): values and value in global governance*. 2020.
9. Abbey EJ, Khalifa BA, Oduwole MO, Ayeh SK, Nudotor RD, Salia EL, et al. The Global Health Security Index is not predictive of coronavirus pandemic responses among Organization for Economic Cooperation and Development countries. *PLoS One* 2020;**15**(10):e0239398.
10. Aitken T, Chin KL, Liew D, Ofori-Asenso R. Rethinking pandemic preparation: Global Health Security Index (GHSI) is predictive of COVID-19 burden, but in the opposite direction. *J Infect* 2020;**81**(2):318.
11. Boyd MJ, Wilson N, Nelson C. Validation analysis of global health security index (GHSI) scores 2019. *BMJ Glob Health* 2020;**5**(10):e003276.
12. Bandelow NC, Hassenteufel P, Hornung J. Patterns of democracy matter in the COVID-19 crisis. *Rev Publ Policy* 2021:121.
13. Gokmen Y, Baskici C, Ercil Y. The impact of national culture on the increase of COVID-19: a cross-country analysis of European countries. *Int J Intercult Relat* 2021;**81**:1–8.
14. Verguet S, Hailu A, Eregata GT, Memirie ST, Johansson KA, Norheim OF. Toward universal health coverage in the post-COVID-19 era. *Nat Med* 2021;**27**(3):380–7.
15. Lal A, Erondu NA, Heymann DL, Gitahi G, Yates R. Fragmented health systems in COVID-19: rectifying the misalignment between global health security and universal health coverage. *Lancet* 2021;**397**(10268):61–7.
16. Geddes B, Wright J, Frantz E. New data set: autocratic breakdown and regime transitions. *Perspect Polit* 2014;**12**(2):313–31.
17. Haber S. *Authoritarian government. The Oxford handbook of political economy*. 2006. p. 693–707.
18. Theuns T. Pluralist democracy and non-ideal democratic legitimacy: against functional and global solutions to the boundary problem in democratic theory. *Democr Theory* 2021;**8**(1):23–49.
19. Pasquino G. Populism and democracy. In: Albertazzi D, McDonnell D, editors. *Twenty-first century populism*. London: Palgrave Macmillan; 2008. p. 15–6.
20. Henry JF. The ideology of the Laissez Faire Program. *J Econ Issues* 2008;**42**(1):209–24.
21. Kaufmann D, Kraay A. *The worldwide governance indicators (WGI) project*. 2020. http://info.worldbank.org/governance/wgi/. [Accessed 16 October 2021].
22. Hofstede G. Dimensionalizing cultures: the Hofstede model in context. *Online Read Psychol Cult* 2011;**2**(1). 2307-0919.1014.
23. Hofstede G, Bond MH. Hofstede's culture dimensions: an independent validation using Rokeach's value survey. *J Cross Cult Psychol* 1984;**15**(4):417–33.
24. Jackson T. In: *The legacy of Geert Hofstede*, vol. 20. London: SAGE Publications; 2020. p. 3–6.
25. Jones JM. *Objective lists – country similarity*. 2020. https://objectivelists.com/2020/05/30/country-similarity-index/. [Accessed 17 October 2021].
26. Raymaekers J, Verbeke W, Verdonck T. Weight-of-evidence through shrinkage and spline binning for interpretable nonlinear classification. *Appl Soft Comput* 2022;**115**:108160.
27. World Health Organisation. Maternal, newborn, child and adolescent health and ageing data portal. https://www.who.int/data/maternal-newborn-child-adolescent-ageing/indicator-explorer-new/mca/uhc-service-coverage-index-(sdg-3.8.1). Accessed October 21, 2021.
28. Teh JK, Bradley DA, Chook JB, Lai KH, Ang WT, Teo KL, et al. Multivariate visualization of the global COVID-19 pandemic: a comparison of 161 countries. *PLoS One* 2021;**16**(5):e0252273.
29. The World Bank. *The World Bank open data*. 2022. https://data.worldbank.org/. [Accessed 15 October 2021].

30. GitHub. *Data on COVID-19 (coronavirus) by our world in data*. https://github.com/owid/covid-19-data/tree/master/public/data. [Accessed 21 October 2021].
31. European Centre for Disease Prevention and Control (ECDC). *Download historical data (to 14 December 2020) on the daily number of new reported COVID-19 cases and deaths worldwide*. 2020. https://www.ecdc.europa.eu/en/publications-data/download-todays-data-geographic-distribution-covid-19-cases-worldwide. [Accessed 16 October 2021].
32. Australian Government Department of Health. *Coronavirus (COVID-19) at a glance – 1 January 2021*. 2021. https://www.health.gov.au/resources/publications/coronavirus-covid-19-at-a-glance-1-january-2021. [Accessed 16 October 2021].
33. Australian Government Department of Health. *Coronavirus (COVID-19) – New Zealand – situation update as at 6 January 2021*. 2021. https://www.health.gov.au/resources/publications/coronavirus-covid-19-new-zealand-situation-up-date-as-at-6-january-2021. [Accessed 16 October 2021].
34. National Health Commission of the People's Republic of China. Outbreak notification the latest situation of the novel coronavirus pneumonia as of 24:00 on December 31. http://www.nhc.gov.cn/xcs/yqtb/202101/fb6984369cf24060b5d4187e7fa3fc53.shtml. Accessed 16 October, 2021.
35. World Health Organization (WHO). *COVID-19 in Viet Nam situation report 24*. 2020. https://www.who.int/vietnam/internal-publications-detail/covid-19-in-viet-nam-situation-report-24. [Accessed 16 October 2021].
36. World Health Organization (WHO). *WHO health emergency dashboard (COVID-19) Samoa*. https://covid19.who.int/region/wpro/country/ws, 2020. [Accessed 16 October 2021].
37. World Health Organization (WHO) Commentaries. Modes of transmission of virus causing COVID-19: implications for IPC precaution recommendations. *Sci Brief* 2020;**369**:1. https://www.who.int/news-room/commentaries/detail/modes-of-transmission-of-virus-causing-covid-19-implications-for-ipc-precaution-recommendations. [Accessed 3 February 2022].
38. Mahase E. Covid-19: what is the R number? *BMJ* 2020;**369**:m1891.
39. *Coronavirus pandemic (COVID-19)*. 2020. https://ourworldindata.org/coronavirus. [Accessed 9 May 2023].
40. Healthline. *Here's exactly where we are with vaccines and treatments for COVID-19*. 2021. https://www.healthline.com/health-news/heres-exactly-where-were-at-with-vaccines-and-treatments-for-covid-19. [Accessed 13 January 2022].
41. Institute for Economic and Peace. *Public release data*. 2022. https://www.visionofhumanity.org/public-release-data/. [Accessed 16 October 2021].
42. The World Bank. GDP (current US$)-High income, Middle income, Low income. https://data.worldbank.org/indicator/NY.GDP.MKTP.CD?locations=XD-XP-XM Accessed October 21, 2021.
43. The World Bank. Current health expenditure (% of GDP). https://data.worldbank.org/indicator/SH.XPD.CHEX.GD.ZS?most_recent_value_desc=true Accessed October 21, 2021.
44. Alexander KA, Sanderson CE, Marathe M, Lewis BL, Rivers CM, Shaman J, et al. What factors might have led to the emergence of Ebola in West Africa? *PLoS Neglect Trop Dis* 2015;**9**(6):e0003652.
45. The World Bank. Population density (people per sq. km of land area). https://data.worldbank.org/indicator/EN.POP.DNST?most_recent_value_desc=true. Accessed October 21, 2021.
46. The World Bank. Physicians (per 1,000 people). https://data.worldbank.org/indicator/SH.MED.PHYS.ZS Accessed October 21, 2021.
47. The World Bank. Hospital bed (per 1,000 people). https://data.worldbank.org/indicator/SH.MED.BEDS.ZS Accessed October 21, 2021.
48. Galston WA. The populist challenge to liberal democracy. *J Democr* 2018;**29**(2):5–19.
49. Ledesma JR, Isaac CR, Dowell SF, Blazes DL, Essix GV, Budeski K, et al. Evaluation of the Global Health Security Index as a predictor of COVID-19 excess mortality standardised for under-reporting and age structure. *BMJ Glob Health* 2023;**8**(7):e012203.
50. Taylor S. *The psychology of pandemics: preparing for the next global outbreak of infectious disease*. Cambridge Scholars Publishing; 2019.
51. George DB, Taylor W, Shaman J, Rivers C, Paul B, O'Toole T, et al. Technology to advance infectious disease forecasting for outbreak management. *Nat Commun* 2019;**10**(1):1–4.
52. Desai AN, Kraemer MU, Bhatia S, Cori A, Nouvellet P, Herringer M, et al. Real-time epidemic forecasting: challenges and opportunities. *Health Sec* 2019;**17**(4):268–75.
53. Oppenheim B, Gallivan M, Madhav NK, Brown N, Serhiyenko V, Wolfe ND, et al. Assessing global preparedness for the next pandemic: development and application of an epidemic preparedness index. *BMJ Glob Health* 2019;**4**(1):e001157.
54. Haider N, Yavlinsky A, Chang Y-M, Hasan MN, Benfield C, Osman AY, et al. The Global Health Security index and Joint External Evaluation score for health preparedness are not correlated with countries' COVID-19 detection response time and mortality outcome. *Epidemiol Infect* 2020:148.
55. Quinn SC, Kumar S. Health inequalities and infectious disease epidemics: a challenge for global health security. *Biosecur Bioterror Biodefense Strat Pract Sci* 2014;**12**(5):263–73.
56. Daszak P, Keusch GT, Phelan AL, Johnson CK, Osterholm MT. Infectious disease threats: a rebound to resilience: commentary reviews the US approach to pandemic preparedness, its impact on the response to COVID-19, and offers policy options to strengthen US pandemic resilience. *Health Aff* 2021;**40**(2):204–11.
57. Fisher D, Teo YY, Nabarro D. Assessing national performance in response to COVID-19. *Lancet* 2020;**396**(10252):653–5.
58. Australian Government Department of Health and Aged Care. *Coronavirus (COVID-19) pandemic*. 2020. https://www.health.gov.au/health-alerts/covid-19#:~:text=On%2025%20February%202020%2C%20the,19%20to%20be%20a%20pandemic. [Accessed 17 July 2023].
59. Galvani AP, Parpia AS, Pandey A, Zimmer C, Kahn JG, Fitzpatrick MCJE. *The imperative for universal healthcare to curtail the COVID-19 outbreak in the USA*. 2020. p. 23.
60. Johnson BB, Swedlow B. Comparing cultural theory and cultural cognition theory survey measures to each other and as explanations for judged risk. *J Risk Res* 2020;**23**(10):1278–300.
61. Van Bavel JJ, Pereira A. The partisan brain: an identity-based model of political belief. *Trends Cognit Sci* 2018;**22**(3):213–24.
62. Chaurasia V, Pal S. *Application of machine learning time series analysis for prediction COVID-19 pandemic*. 2020. p. 1–13.

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Original Research

Evaluation of food security status, psychological well-being, and stress on BMI and diet-related behaviors among a sample of college students

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ABSTRACT

Objectives: The purpose of this study was to evaluate food insecurity on body mass index (BMI) and diet-related behaviors among college students and whether psychological well-being (PWB) and stress levels mediate this relationship.
Study design: This was a cross-sectional study.
Methods: Data from 1439 students from the American College Health Association National College Health Assessment III (Fall 2020) were used. Food security status was evaluated by the USDA Six-Item Short Form. PWB was measured using the Diener Flourishing Scale. Diet-related behaviors included the average servings of fruits, vegetables, and sugar-sweetened beverages consumed per day. Stress was measured by self-reported levels. Regression model analysis evaluated the influence of food security status, PWB, and stress levels on BMI. PWB and stress were also tested as mediators in the relationship between food insecurity and BMI.
Results: Among our sample of college students, 44.54% ($n = 641$) were food insecure, and 55.46% ($n = 798$) were food secure. Multiple regression analysis showed that higher food insecurity, older age, full-time enrollment status, and fifth-year student status were positively associated with a higher BMI score ($P < 0.05$). Results from mediation models revealed that PWB, but not stress, mediated the relationship between food security and BMI among Black/African American students. Regarding diet-related behaviors, high stress levels mediated the relationship between food insecurity and sugar-sweetened beverage intake among students.
Conclusions: Food insecurity appears to influence BMI in college students. This relationship seems to be mediated by disrupted PWB and a higher intake of sugar-sweetened beverages due to stress.

Introduction

College students are in a unique position as young adults with newfound independence, and one that comes with a significant number of responsibilities. Most college students (62.7%) begin college within months following high school graduation.[1] Upon attending college, these students are responsible for more than just learning. For many, the responsibility of managing the financial expenses required to attend college, including housing and tuition, as well as the basics of living, such as regular food intake, sleep schedule, and more, can be overwhelming. Most first-year college students (83.8%) receive some form of financial aid to assist with academic expenses.[2] Financial and adaptive stressors in the college population have been suggested as precursors of food insecurity.

Food insecurity refers to inconsistent access to enough food to meet basic needs, which typically occurs due to a lack of money or other resources.[3] According to a systematic review, an estimated 32.9% of all college students in the USA experience food insecurity (short and long term).[4] The prevalence of food insecurity in college students is higher than the national average reported for all US households (with and without children), which peaked at 14.7% as a result of the Great Recession[5] but has been below 14% since

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recovery from this nationwide economic hardship. As of 2021, an average of 10.2% of US households were food insecure.[3] Food insecurity among college students is both a growing humanitarian concern and a health concern, as these students have been found to experience more negative physical and mental health consequences than their food-secure peers.

Food-insecure college students tend to report overall poorer dietary quality than food-secure peers,[6,7] including skipping meals, particularly breakfast,[6,8,9] consuming more foods and beverages with added sugars,[7] and consuming fewer fruits and vegetables.[6,7,9–14] In addition to less healthy dietary behavior, food-insecure college students have reported less physical activity than their peers as well as insufficient sleep.[6] Notably, food insecurity is associated with five times greater odds of obesity in college students.[7] However, a mechanism between food security status and body mass index (BMI) outcomes is not clear.

Food insecurity in college students is also related to aspects of emotional health,[15–17] such as higher rates of anxiety, depression, stress, and/or psychological well-being (PWB).[6,18] While the general college student population has long been found to experience some degree of stress,[19–21] it has recently been recognized that food-insecure college students have two times higher odds of experiencing stress than students who do not have this struggle to meet basic needs.[6] Furthermore, reported stress among college students has been found to increase as the severity of food insecurity increases.[18] Differences between students with food insecurity have also been observed in PWB, a measure that encompasses characteristics that give meaning or purpose to an individual's life, such as positive social relationships, values, and other factors contributing to a fulfilling quality of life.[22–24]

The purpose of this study was to evaluate the influence of food insecurity in BMI and diet-related behaviors among college students while also exploring the potential influence of PWB and stress in this relationship. Specifically, the first aim of the present study was to evaluate the differences in student characteristics by food-security status (food secure/food insecure). The second aim was to evaluate whether food insecurity, PWB, and stress were associated with BMI and diet-related behaviors (intake of fruit, vegetables, and sugar-sweetened beverages). Finally, the third aim was to evaluate the influence of PWB and stress as mediators in the relationship between food security and BMI. We hypothesized that college students with food insecurity would exhibit a higher BMI in comparison to food-secure students and that low PWB and high stress would be negatively associated with BMI and diet-related behaviors (meaning a higher BMI, lower intake of fruits and vegetables, and higher intake of sugar-sweetened beverages).

Methods

Population

Approximately 8000 undergraduate students from a large public university in the southeastern region of the USA were invited to participate in the Fall 2020 American College Health Association National College Health Assessment (ACHA-NCHA III) survey. The total respondents numbered 1516 students. Due to very small sample sizes, students who were classified into the categories of American Indian, Middle Eastern, and Native Hawaiian were excluded. This study included data from a total of 1439 respondents.

The general demographic data of respondents are presented by food-security status (food security vs food insecurity) in Table 1. Data were de-identified before the investigator received them. The Institutional Review Board for Human Use (IRB) at the University of Alabama at Birmingham approved this study (IRB-300009705).

Measures

The NCHA data set includes an extensive collection of measures (see NCHA III Codebook via acha.org), including variables of relevance for the current study analyses as detailed below.

Demographics

Demographic information included gender, race/ethnicity, student status, enrollment status, housing, age, financial challenges, and COVID-19 variables. These data were collected via the following questions: ‘which term do you use to describe your gender identity?’ (gender), ‘how do you usually describe yourself?’ (race/ethnicity), ‘what is your year in school?’ (student status), ‘what is your enrollment status?’ (enrollment status), ‘where do you currently live?’ (housing), ‘how old are you’ (age), “within the last 12 months, have you had problems or challenges with ….?’ (financial challenges), ‘have you had COVID-19?’ (COVID-19 diagnosis), and ‘how has your current overall level of stress been impacted by the COVID-19 pandemic?’ (level of stress impacted by COVID-19).

Food security

Food security was assessed using the United States Department of Agriculture (USDA) Six-Item Short Form of the Food Security Survey Module. Affirmative responses were scored according to USDA guidelines, and respondents with cumulative scores >2 (range 0–6) were classified as food insecure.[25]

Stress levels

Stress levels were assessed with the question ‘within the last 30 days, how would you rate the overall level of stress you have experienced?’ Response options included no stress, low stress, moderate stress, and high levels of stress.

Psychological well-being

PWB was measured with the Diener Flourishing Scale.[22] This scale includes eight statements with which respondents may agree or disagree on a Likert scale (strongly disagree (1), disagree (2), slightly disagree (3), neither agree nor disagree (4), slightly agree (5), agree (6), strongly agree (6)). Examples of these statements include: ‘I lead a purposeful and meaningful life,’ ‘my social relationships are supportive and rewarding,’ etc. Responses are scored according to published guidelines, and respondents are given a total score between eight and 56, with higher scores indicating more psychological resources and strengths.[22]

Physical activity

Physical activity was measured by self-reported minutes of moderate aerobic activity (brisk walking, dancing, or household chores) and vigorous aerobic activity (running, swimming laps, or hiking) within the last seven days. Self-reported strength training (push-ups, sit-ups, or weightlifting/training) within the last seven days was also included.

Diet-related behaviors

Dietary patterns were assessed by self-reported servings of fruit, vegetables, and sugar-sweetened beverages consumed. Respondents reported average consumption in the last seven days in fill-in-the-blank questions.

Table 1
Demographic characteristics by food-security status among a sample of college students (n = 1439).

Variables	Total	Food insecure (44.54%)	Food secure (55.46%)	*P*-value
Percentage (n)				
Gender (n = 1406)				**0.0157**
Female	70.55% (n = 992)	72.57% (n = 455)	68.93% (n = 537)	
Male	26.74% (n = 376)	23.76% (n = 149)	29.14% (n = 227)	
Non-binary	2.70% (n = 38)	3.67% (n = 23)	1.93% (n = 15)	
Race/ethnicity (n = 1379)				**0.0347**
White	58.81% (n = 811)	58.12% (n = 358)	59.37% (n = 453)	
Asian or Asian American	9.79% (n = 135)	7.63% (n = 47)	11.53% (n = 88)	
Black or African American	20.59% (n = 284)	23.54% (n = 145)	18.22% (n = 139)	
Hispanic or Latino/a/x	3.84% (n = 53)	4.06% (n = 25)	3.67% (n = 28)	
Biracial or Multiracial	6.96% (n = 96)	6.66% (n = 41)	7.21% (n = 55)	
Student status (n = 1407)				**0.0161**
1st year	24.52% (n = 345)	20.86% (n = 131)	27.47% (n = 214)	
2nd year	19.76% (n = 278)	21.18% (n = 133)	18.61% (n = 145)	
3rd year	24.09% (n = 339)	27.07% (n = 170)	21.69% (n = 169)	
4th year	22.53% (n = 317)	21.50% (n = 135)	23.36% (n = 182)	
5th year	9.10% (n = 128)	9.39% (n = 59)	8.86% (n = 69)	
Enrollment status (n = 1404)				0.6678
Full-time	88.46% (n = 1242)	88.52% (n = 555)	88.42% (n = 687)	
Part-time	11.47% (n = 161)	11.48% (n = 72)	11.45% (n = 89)	
Other	0.07% (n = 1)	0.00% (n = 0)	0.07% (n = 1)	
Housing (n = 1402)				**<0.0001**
Campus or university housing	30.60% (n = 429)	26.72% (n = 167)	33.72% (n = 262)	
Parent/guardian/other family Members	29.39% (n = 412)	26.88% (n = 168)	31.40% (n = 244)	
Off-campus	37.80% (n = 530)	44.00% (n = 275)	32.82% (n = 255)	
Temporarily staying with a relative/friend	0.64% (n = 9)	1.12% (n = 7)	0.26% (n = 2)	
Other	1.57% (n = 22)	1.28% (n = 8)	1.80% (n = 14)	
Age (n = 1391)				0.0638
18–22 years	79.80% (n = 1110)	79.52% (n = 497)	80.03% (n = 613)	
23–27 years	9.20% (n = 128)	10.88% (n = 68)	7.83% (n = 60)	
>28 years	11.00% (n = 153)	9.60% (n = 60)	12.14% (n = 93)	
Financial challenges (n = 1404)				**<0.0001**
Yes	48.93% (n = 687)	67.69% (n = 465)	32.31% (n = 222)	
No	51.07% (n = 717)	22.45% (n = 161)	77.55% (n = 556)	
COVID-19 (positive diagnosis) (n = 1007)				0.7366
Yes	6.45% (n = 65)	56.92% (n = 28)	43.08% (n = 37)	
No	93.55% (n = 942)	54.78% (n = 516)	45.22% (n = 426)	
Mean ± STD				
Age (n = 1418)	22.15 ± 6.56	21.81 ± 5.54	22.32 ± 7.06	0.1335
BMI (n = 1392)	26.40 ± 7.14	27.32 ± 7.62	25.64 ± 6.69	**<0.0001**
Stress, psychological well-being, physical activity, and diet				
Stress (n = 1406)				**<0.0001**
No stress	2.06% (n = 29)	0.80% (n = 5)	3.08% (n = 24)	
Low stress	18.49% (n = 260)	11.31% (n = 71)	24.29% (n = 189)	
Moderate stress	50.07% (n = 704)	48.41% (n = 304)	51.41% (n = 400)	
High stress	29.37% (n = 413)	39.49% (n = 248)	21.21% (n = 165)	
Mean ± STD				
Psychological well-being (n = 1425)	45.29 ± 8.46	43.88 ± 9.02	46.50 ± 7.67	**<0.0001**
Physical activity				
Moderate physical activity (average minutes last 7 days) (n = 1426)	225.08 ± 409.92	227.11 ± 415.18	220.30 ± 373.43	0.7470
Vigorous physical activity (average minutes last 7 days) (n = 1418)	79.81 ± 173.37	78.02 ± 193.36	80.64 ± 156.01	0.7799
Days of strength exercise (n = 1406)	1.51 ± 1.89	1.45 ± 1.88	1.56 ± 1.89	0.2424
Diet-related Behaviors (Servings per day) (n = 1431)				
Fruits	2.01 ± 0.71	1.99 ± 0.67	2.02 ± 0.74	0.4056
Vegetables	2.21 ± 0.77	2.19 ± 0.74	2.22 ± 0.79	0.4782
Sugar-sweetened beverages	3.10 ± 4.44	3.43 ± 4.67	2.87 ± 4.28	**0.0187**

Differences were analyzed using t-test (quantitative variables) and chi-squared (categorical variables) tests. Significant differences were denoted at $P < 0.05$.

Body mass index

BMI was computed based on self-reported height and weight. The calculation for computing BMI is weight (kg)/(height (m))^2. BMI was reported as both a continuous and a categorical variable (underweight, normal weight, overweight, or obese).

Statistical analysis

Descriptive statistics (mean, standard deviation,[25] and frequencies) were calculated to summarize gender (female, male, and non-binary), self-reported race/ethnicity (White, Asian or Asian American, Black or African American, Hispanic or Latino/a/x, and biracial or multiracial), students status (first, second, third, fourth, and fifth year), enrollment status (full-time, part-time, and other), housing (campus or university housing, parent/guardian/other family members, off-campus, temporarily staying with a relative/friend, and other), age (reported in years), financial challenges (yes/no), COVID-19 positive diagnosis (yes/no), BMI (m/kg^2), BMI classification (underweight, normal weight, overweight, or obese), stress level (no, low, moderate, or high stress), PWB (scores between eight and 56), physical activity (average minutes of physical activity during last seven days and days of strength exercise), and diet characteristics (average serving of fruits, vegetables, and sugar-sweetened beverage per day) by food security status (food secure vs food insecure). Differences for absolute values in demographic characteristics between food-secure and food-insecure students were analyzed using t-tests and chi-squared tests.

The testing of our hypothesis was based on the identification of the most parsimonious statistical model balancing the variables of interest. Multiple regression analyses were performed to evaluate the impact of food security, PWB, and stress on the BMI of all students, then on the BMI of students classified as overweight or obesity specifically (with and without comorbidities) and on sugar-sweetened beverage intake (fruit and vegetable intake were not included since there were no differences by food security status). Multiple regression models were adjusted by age, gender (male as the reference group), enrollment status (full-time as the reference group), year in school (fifth year as the reference group), housing (campus housing as the reference group), physical activity (minutes of doing moderate physical activity in the last seven days), and race (White students as the reference group). All residuals were tested for normality after visual evaluation (residuals ± 3 standard deviations were removed from the regression models).

Simple mediation models were conducted to evaluate the influence of PWB and stress on the relationship between food insecurity and obesity. Simple mediation was conducted according to the bootstrapping technique. Bootstrapping is a statistical approach in which cases from the original data set are randomly re-sampled with replacement to re-estimate the sampling distribution. From the sampling distribution, confidence intervals (CIs) are then constructed. A conditional indirect effect is considered 'significant' if zero is not contained within the upper and lower CIs.[26] PWB and stress were tested as mediators in the relationship between food insecurity and BMI. The following models were proposed: 1) Model 1: The relationship between food insecurity and BMI will be mediated by PWB scores (Model 1a) and level of stress (Model 1b); and 2) Model 2: The relationship between food insecurity and dietary intake of fruits (Model $2a_{1(PWB)}$/Model $2b_{1(stress)}$), vegetables (Model $2a_{2(PWB)}$/Model $2b_{2(stress)}$), and sugar-sweetened beverages (Model

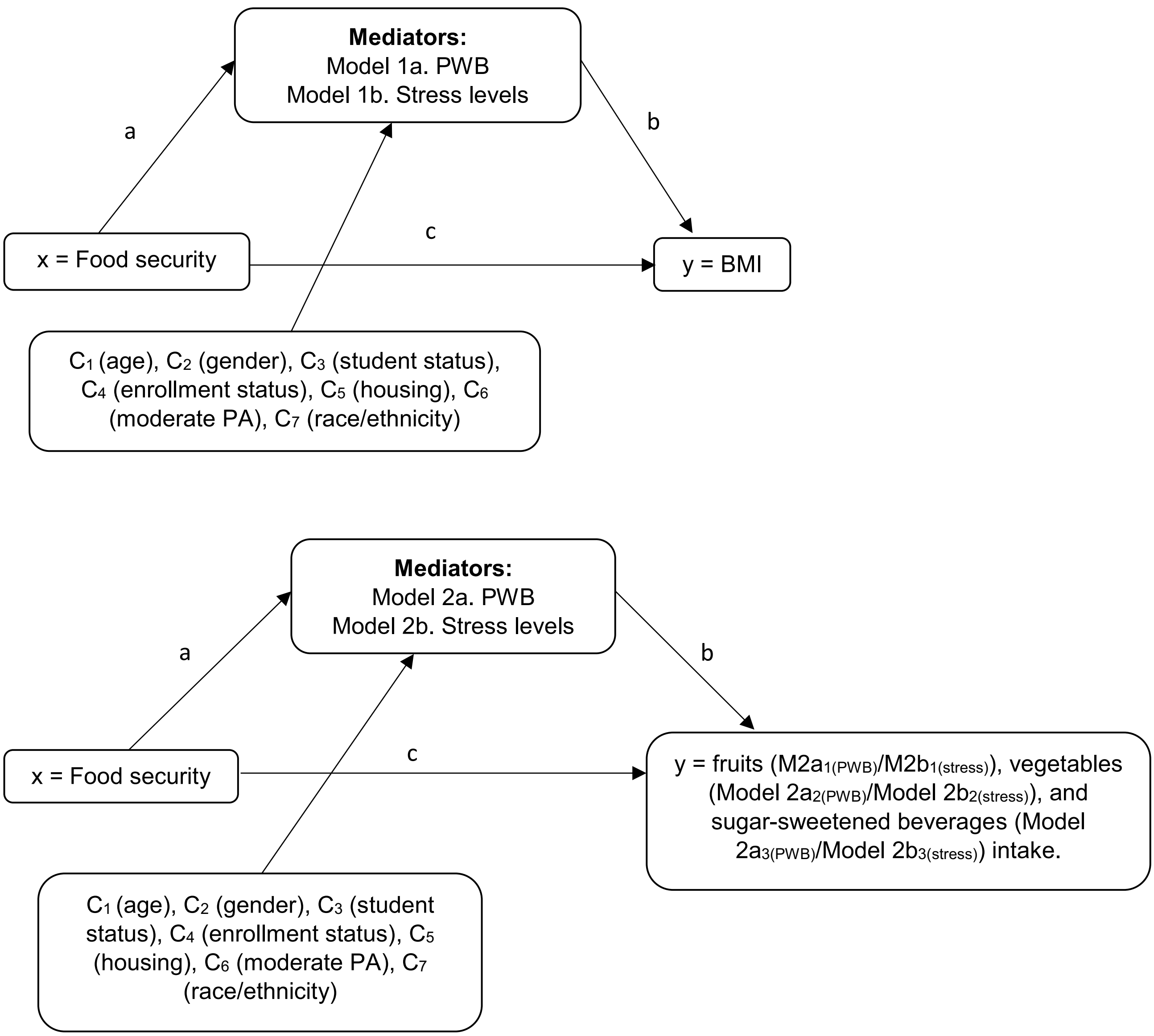

Fig. 1. Mediation models.
Simple mediation. Conceptual models (models 1a and 1b) showing the direct path (c) and mediated path (a and b) between food security and BMI controlled by covariates.
Simple mediation. Conceptual models (models 2a and 2b) showing the direct path (c) and mediated path (a and b) between food security and diet (fruits, vegetables, and sugar-sweetened beverages intake) controlled by covariates.

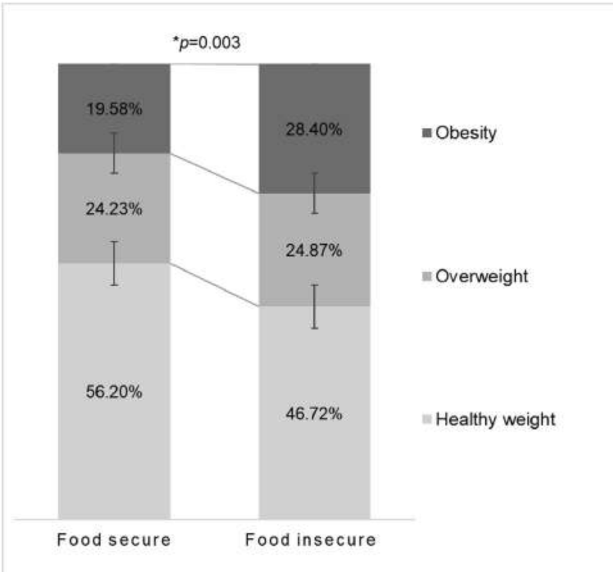

Fig. 2. BMI classification by food-security status (food secure/food insecure) in a sample of college students.

$2a_{3(PWB)}$/Model $2b_{3(stress)}$) will be mediated by PWB scores (Models $2a_{(1\text{-}3)}$) and level of stress (Models $2b_{(1\text{-}3)}$) (see Fig. 1).

Missing values were treated by complete case analysis, in which missing values were excluded from the analysis. The significance level was considered $\alpha = 0.05$ for all statistical analyses. All analyses were performed with SAS statistical software (version 9.4, 2002–2012 by SAS Institute Inc., Cary, NC).

Results

Demographic characteristics

The demographic characteristics of our sample are summarized in Table 1 by food security status. From the total sample (n = 1439), college students ages 18–69 years were included. Most of the students in our sample were female (gender), White (race), in their first year of study (student status), full-time students (enrollment status), and living off-campus (housing). Significant differences were observed for gender, race/ethnicity, student status, housing, financial challenges, and BMI scores ($P < 0.05$). A total of 23.42% (n = 326) of the students were overweight, and 22.63% (n = 315) exhibited obesity according to their BMI. Regarding stress, PWB, physical activity, and diet characteristics, significant differences were observed in levels of stress, PWB, and sugar-sweetened beverage intake by food security status ($P < 0.05$).

Relationship between food security, psychological well-being, stress, and BMI

Among this sample of college students, 44.54% were food insecure, while 55.46% were food secure. Significant differences were seen when considering BMI classification by food-security status, such that a higher percentage of individuals with obesity was observed among food-insecure college students ($P = 0.0003$) (Fig. 2).

Table 2 shows results for the multiple regression models assessing the contribution of food security, PWB, and stress on both BMI (students with overweight/obesity [BMI >24.9 kg/m^2] only) and intake of sweetened beverages. Multiple regression models were adjusted for age, gender, student status, enrollment status, housing, physical activity, and race/ethnicity. All analyses yielded statistically significant models ($P < 0.05$). High food-security scores (being food secure), older age, being a full-time student, and being White, Asian/Asian American, or Black/African American (each group was compared to the entire population) were positively associated with higher BMI scores ($P < 0.05$). Considering only those with overweight and obesity (with and without comorbidities), high food-security scores, older age, and being White or Black/African American (each group was compared to the entire population) were positively associated with their BMI ($P < 0.05$). Finally, high food-security scores, high stress, and being White or Asian/Asian American (each group was compared to the entire population) were positively associated with a higher intake of sugar-sweetened beverages ($P < 0.05$). Physical activity

Table 2
Multiple regression analysis testing the effect of food security, psychological well-being, and stress on BMI among all students, on BMI in students with overweight or obesity (with and without comorbidities), and on sugar-beverage intake in a sample of multiracial college students.

Variables (n = 1439)	BMI (kg/m^2)		BMI (kg/m^2) in students with overweight and obesity (with and without comorbidities)		Sugar-sweetened beverage intake	
	F([11,1276] = 15.63, $P < 0.0001$, $R^2 = 0.1196$)		F([10,590] = 4.81, $P < 0.0001$, $R^2 = 0.0608$)		F([10,1216] = 3.43 $P = 0.0002$, $R^2 = 0.0277$)	
	β	*P*-value	β	*P*-value	β	*P*-value
Food security	0.2638	**0.0003**	0.22194	**0.0278**	0.06651	**0.0171**
Psychological well-being	−0.03387	0.0789	−0.01921	0.4655	−0.0000982	0.9893
Stress level (high)	−0.11666	0.7464	0.03526	0.943	0.31787	**0.022**
Covariates						
Age	0.21881	**<0.0001**	0.11969	**0.0003**	−0.01384	0.2092
Gender (male)	0.35909	0.2992	−0.59194	0.214	0.20142	0.1263
Enrollment status (full-time)	−1.6027	**0.0051**	−0.20858	0.7525	0.15136	0.4831
Year in school (5th year)	0.8315	0.1468	0.15859	0.8128	0.14038	0.5099
Housing (campus)	−0.14563	0.685	−0.14489	0.7819	0.14035	0.3052
Physical activity (minutes moderate PA)	−0.00119	**0.0029**	−0.00179	**0.0416**	−0.0003736	**0.0136**
Race (White)	−0.66139	**0.0352**	−1.51585	**0.0005**	−0.25645	**0.0302**

All models adjusted for age, gender, race, student status, enrollment students, and housing. Models use male, full-time, 5th-year, campus housing, and White students as reference groups. Significant differences were denoted at $P < 0.05$.
Differences were analyzed using chi-squared test. Significant differences were denoted at $P < 0.05$.

(moderate PA) was negatively associated with BMI scores in the entire sample and in those with overweight or obesity ($P = 0.0029$ and $P = 0.0416$, respectively). In addition, moderate PA was associated with a lower intake of sugar-sweetened beverages ($P = 0.0302$).

Simple mediation models

The models evaluating the mediation role of PWB in the relationship between food insecurity and BMI (Model 1a) and the mediation role of levels of stress in the relationship between food insecurity and sugar-sweetened beverage intake (Model $2b_3$) showed statistically significant results ($P < 0.05$). Models evaluating the mediation role of level of stress on the relationship between food insecurity and BMI (Model 1b) and the mediation role of PWB in the relationship between food insecurity and dietary intake of fruits (Model $2a_1$), vegetables (Model $2a_2$), and sugar-sweetened beverages (Model $2a_3$) and the mediation role of levels of stress in the relationship between food insecurity and dietary intake of fruits (Model $2b_1$) and vegetables (Model $2b_2$) were not statistically significant (data not shown).

Model 1a hypothesized that PWB mediates the relationship between food insecurity and BMI. To test this hypothesis, confidence intervals (CIs, 95%) were generated. Results of the indirect effect, based on a bootstrapped sample of 1,000, revealed that zero was contained within the lower and upper limits in White, Asian/Asian American, Hispanic or Latino/a/x, and multiracial students, indicating that PWB did not mediate the relationship between food insecurity and BMI. However, among Black/African American students, PWB mediates the relationship between food insecurity and

Table 3

Unstandardized coefficients for psychological well-being as mediator in the relationship between food security and BMI (model 1a), and for stress as mediator in the relationship between food security and sugar-sweetened beverages intake (model $2b_3$) in a sample of college students controlled by covariates.

Path		β-coefficient	SE	t	*P*-value
Model 1a					
White					
Food security to psychological well-being	a1	−0.5984	0.1069	−5.5975	**<0.0001**
Psychological well-being to BMI	b1	−0.0322	0.0186	−1.735	0.083
Food security to BMI	c	0.2785	0.0709	3.9281	**0.0001**
Indirect effect CI (−0.0035, 0.0447)					
Asian or Asian American					
Food security to psychological well-being	a1	−0.5937	0.107	−5.5483	**<0.0001**
Psychological well-being to BMI	b1	−0.0316	0.0185	−1.7059	0.0883
Food security to BMI	c	0.2696	0.0706	3.8167	**0.0001**
Indirect effect CI (−0.0039, 0.0421)					
Black or African American					
Food security to psychological well-being	a1	−0.6273	0.1071	−5.8569	**<0.0001**
Psychological well-being to BMI	b1	−0.0389	0.0185	−2.1074	**0.0353**
Food security to BMI	c	0.2468	0.0706	3.4938	**0.0005**
Indirect effect CI (0.0009, 0.0499)					
Hispanic or Latino/a/x					
Food security to psychological well-being	a1	−0.5912	0.1068	−5.5354	**<0.0001**
Psychological well-being to BMI	b1	−0.0309	0.0186	−1.6613	0.0969
Food security to BMI	c	0.2854	0.0709	4.0255	**0.0001**
Indirect effect CI (−0.0043, 0.0427)					
Biracial or Multiracial					
Food security to psychological well-being	a1	−0.5934	0.1066	−5.564	**<0.0001**
Psychological well-being to BMI	b1	−0.0312	0.0186	−1.6724	0.0947
Food security to BMI	c	0.2866	0.0709	4.0426	**0.0001**
Indirect effect CI (−0.0048, 0.0426)					
Model $2b_3$					
White					
Food security to stress	a1	0.0834	0.0092	9.0472	**<0.0001**
Stress to sugar-sweetened beverages	b1	0.4554	0.1767	2.5777	**0.0101**
Food security to sugar-sweetened beverages	c	0.1775	0.0581	3.0547	**0.0023**
Indirect effect CI (0.0097, 0.0672)					
Asian or Asian American					
Food security to stress	a1	0.0827	0.0092	8.9555	**<0.0001**
Stress to sugar-sweetened beverages	b1	0.4703	0.1762	2.6693	**0.0077**
Food security to sugar-sweetened beverages	c	0.168	0.0581	2.8917	**0.0039**
Indirect effect CI (0.0107, 0.0687)					
Black or African American					
Food security to stress	a1	0.0859	0.0092	9.3031	**<0.0001**
Stress to sugar-sweetened beverages	b1	0.4771	0.1772	2.6922	**0.0072**
Food security to sugar-sweetened beverages	c	0.1714	0.0584	2.9352	**0.0034**
Indirect effect CI (0.0106, 0.0691)					
Hispanic or Latino/a/x					
Food security to stress	a1	0.0826	0.0092	8.9554	**<0.0001**
Stress to sugar-sweetened beverages	b1	0.4556	0.1763	2.5836	**0.0099**
Food security to sugar-sweetened beverages	c	0.1764	0.058	3.0399	**0.0024**
Indirect effect CI (0.0093, 0.0667)					
Biracial or Multiracial					
Food security to stress	a1	0.0824	0.0092	8.9445	**<0.0001**
Stress to sugar-sweetened beverages	b1	0.4609	0.1765	2.6112	**0.0091**
Food security to sugar-sweetened beverages	c	0.1747	0.0581	3.0096	**0.0027**
Indirect effect CI (0.0097, 0.0678)					

Significant differences were denoted at $P < 0.05$.

BMI. Model $2b_3$ hypothesized that stress levels mediate the relationship between food security and sugar-sweetened beverage intake. Results of the indirect effect, based on a bootstrapped sample (n = 1000), revealed that stress mediates the relationship between food security and intake of sugar-sweetened beverages among all races/ethnicities (measured by race/ethnic) (Table 3).

Discussion

The primary aim of this study was to evaluate the influence of food insecurity on BMI and diet-related behaviors in college students. The second aim was to assess whether PWB and stress levels mediated this relationship. The present study accepted the hypothesis that higher food insecurity impacts BMI and that food insecurity and stress influence the intake of sugar-sweetened beverages among college students. Results from mediation models revealed that PWB, but not stress, mediated the relationship between food insecurity and BMI among Black/African American students only. Regarding diet-related behaviors, high stress levels mediated the relationship between food insecurity and sugar-sweetened beverage intake among all college students.

Food insecurity is recognized for contributing to compromised caloric and micronutrient intake, influenced by multiple factors. Based on these present findings, contributions of gender, race/ethnicity, student status, student housing, stress level, PWB, physical activity level, BMI, and consumption of sugar-sweetened beverages appear to contribute to food-security status. These findings suggest that food-insecure students are not a homogenous portion of the undergraduate college student population, and that food insecurity tends to be more prevalent among those who represent socially and financially marginalized sectors of the population. Multiple regression analysis showed that higher food insecurity, older age, full-time enrollment status, and lower PA were positively associated with a higher BMI score ($P < 0.05$). Similar results have previously been seen among US adults after food insecurity increased from 1999 to 2016, and food insecurity was greater in adults with greater adiposity, including those with abdominal obesity.[27] Among college students, it appears that food insecurity in combination with obesogenic behaviors (such as eating large quantities of highly processed foods over healthy food choices) contribute to greater adiposity.[28]

Our results demonstrate a mediation effect of PWB in the relationship between food security and BMI in Black/African American students only. Students of color are known to deal with unique and stressful external challenges and balance such challenges with their own perception of being well in the midst of adversity. Previous evidence has shown that PWB for Black/African Americans is moderated by perceived discrimination and that racism has an impact on their mental health (not assessed in this study).[29,30] There is also research supporting different levels of resilience among individuals as they navigate the college experience,[31] as well as variable perceptions of having a successful and positive outcome (PWB) after completion of their academic pursuits.[32–34] These findings may suggest that some minority students are able to navigate college-related stress with a degree of success, but such successful navigation does not translate into an overall personal sense of PWB.

Stress refers to physical, emotional, or psychological events that occur in an individual's life and the degree to which they respond to the changes they experience.[21] High stress levels mediated the relationship between food insecurity and sugar-sweetened beverage intake among students. Although the behavioral and physiological mechanisms for which food insecurity influences stress and PWB have not been clearly identified, research documents higher odds of stress perception among those who are food insecure, which could potentially mediate a poor relationship between food insecurity and health. Individuals who struggle to meet basic needs often fight a silent, lonely battle. Students who are food insecure are more likely to hide their experiences due to fear of social stigma or shame[35] and are more likely to report feeling lonely.[35,36] Our results bring relevant insight into how stress may be a strong and significant mediator on the relationship between food insecurity and sugar-sweetened beverage intake among students. This observation has the potential to open new venues of exploration into how experiencing perceived stress can increase the hedonic consumption of calorically dense foods, which can, consequently, bring insight into a potential mechanistic role of the sympathetic adrenal medullary system and the hypothalamic-pituitary-adrenal (HPA) axis. Stress stimulates the release of corticotropin-releasing factor from the hypothalamus, which, in turn, stimulates the synthesis of adrenocorticotropic hormone from the anterior pituitary, subsequently triggering the production of glucocorticoids such as cortisol or corticosterone in the adrenal cortex. Repeated and uncontrollable stress can, over time, dysregulate the HPA axis, which, consequently, affects energy homeostasis and eating behavior.[37]

Traditional food insecurity research associates food insecurity with financial stress that influences inconsistent access to enough food to meet basic nutritional needs.[4] The findings of this study demonstrate that the impact food insecurity may have on weight management is complex and multifactorial in nature. Our investigation provides an opportunity to hypothesize a potential role of nutritional and wellness education as a contributor to reduce the impact of food insecurity among college students. The reported stressors faced by college students as they transition into a higher level of decision-making autonomy may impair this population to make judgmental decisions on the accessibility, as well as the quality and quantity, of food needed to achieve nutritional health, a phenomenon that goes beyond financial means. On the other hand, environmental factors such as lack of access to nutritional foods at low cost on college campuses may be impacting health habits. Our findings underscore the importance of research that will better qualify the intrinsic and extrinsic potential influences of factors defining food insecurity and their contribution to overall health, particularly among college students, who quadruple in prevalence of food insecurity when compared to the general population.

As with all epidemiological studies, our investigation is not exempt from limitations. The USDA Six-Item Short Form, although widely used and reputable by its validity and reliability in adult populations, is not a comprehensive tool, and there is a recognized need for a measurement tool specific to college students.[4,38] This study is also limited by the utilization of self-reported data, particularly a stress measure that relies solely on self-perception and the self-report of diet-related behaviors. It is also limited by the exclusion of some racial/ethnic groups due to very small sample size. Furthermore, students' perceptions of food access may have been impacted by the recent COVID-19 pandemic, as data were collected in the fall of 2020. Finally, this study does not account for the dining environment on or near campus that may contribute to obesogenic behaviors. However, the study is strengthened by the substantial sample size and the homogeneity characterized in a college student population, where the standard errors are small, and the parameter estimates for statistical analyses are reduced.

Although food insecurity as a communal phenomenon has been widely studied, the complex etiology of being food insecure seems to require further understanding, particularly when considering that food insecurity does not equally affect all portions of society. An understanding of the factors that underlie such a phenomenon and the impact that it can have on the overall health of a population in need is pivotal. These findings, as well as the cumulation of previously published studies, support the need for college and university programs to support food-insecure college students, as well as state and federal policies. Though financial support is made available to qualifying students through federal financial aid, loans, and grants, this aid is often insufficient at covering the cost of tuition, housing, and other basic financial needs.[39,40] Additionally, though federal programs such as the Supplemental Nutrition Assistance Program (SNAP) are available to American adults in need of food assistance, there are restrictive eligibility requirements that make it difficult for college students to qualify for this monetary benefit towards grocery purchases.[41,42] In an average month, SNAP provided $218 per individual to purchase groceries in 2021,[3] yet college students often do not qualify for this benefit due to the need to meet more eligibility requirements than an adult not enrolled in college courses (e.g., work a minimum of 20 h a week, be responsible for a dependent(s), etc.).[41,42] Expanding the eligibility requirements for SNAP and other federal programs to be more inclusive of college students could help to mitigate the burdensome effects of food insecurity. Additional strategies could be related to the growing evidence in supporting of universal free meals (e.g., in K-12 students), which has been shown to improve academic outcomes as well as healthy weight outcomes.[43–46] Universal free meals are an example of an educational and public health policy with theoretical promise for application in a higher education setting. In the USA, many institutes of higher education require minimum meal plans for students, especially first-year students, and there is evidence that students who have fewer meals in their plan are less food secure.[47] However, it seems that students who worked tended to use their meal plan less, presumably due to working during the hours meal plan meals are available.[47] Further research is needed to determine if students with sufficient meal plans are less food insecure and how changes in student meal plan policies impact food access, academic and healthy weight outcomes. Institutes for higher education may also explore the wellness promotion programs (e.g., those that include activities such as sleep, stress management, and self-care) and food pantries that are available to implement strategies to reduce not only the food insecurity but also to reduce the burden on stress and PWB related to food insecurity.

Research efforts furthering the findings of this study are also needed to reduce the gap in educational and health disparities for this generation and generations to come. These efforts should include interventions to identify and address the underlying causes of food insecurity in college students, including cultural aspects as well as negative health consequences associated with this population experiencing food insecurity. Interventions should use a socio-ecological approach by addressing the societal-level causes of food insecurity as well as actions to address food insecurity per individual college student. This would include consideration of public policies, environmental and community factors, including the college campus community more specifically, and the possible positive influence of social relationships in intervention design and delivery.

Author statements

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Ethical approval

The Institutional Review Board for Human Use (IRB) at the University of Alabama at Birmingham approved this study (IRB-300009705).

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Competing interests

None declared.

References

1. Hanson M. College enrollment & student demographic statistics. Accessed July 26, 2022. https://educationdata.org/college-enrollment-statistics.
2. Hanson M. Financial aid statistics Accessed October 5, 2022. https://educationdata.org/financial-aid-statistics.
3. Coleman-Jensen A, Rabbitt MP, Gregory CA, Singh A. *Statistical supplement to household food security in the United States in 2021*. USDA; 2022. AP(105), https://www.ers.usda.gov/webdocs/publications/104663/ap-105.pdf?v=4529.8.
4. Bruening M, Argo K, Payne-Sturges D, Laska MN. The struggle is real: a systematic review of food insecurity on postsecondary education campuses. *J Acad Nutr Diet. Nov* 2017;**117**(11):1767–91. https://doi.org/10.1016/j.jand.2017.05.022.
5. Nord M, Coleman-Jensen Alisha, Andrews Margaret, Carlson S. *Household food security in the United States*. https://www.ers.usda.gov/publications/pub-details/?pubid=44778; 2009.
6. Bruening M, van Woerden I, Todd M, Laska MN. Hungry to learn: the prevalence and effects of food insecurity on health behaviors and outcomes over time among a diverse sample of university freshmen. *Int J Behav Nutr Phys Activ* 2018;**15**(1):9. https://doi.org/10.1186/s12966-018-0647-7. Jan 18.
7. El Zein A, Colby SE, Zhou W, Shelnutt KP, Greene GW, Horacek TM, et al. Food insecurity is associated with increased risk of obesity in US college students. *Curr Dev Nutr* 2020;**4**(8). https://doi.org/10.1093/cdn/nzaa120.
8. Bruening M, Brennhofer S, van Woerden I, Todd M, Laska M. Factors related to the high rates of food insecurity among diverse, urban college freshmen. *J Acad Nutr Diet. Sep* 2016;**116**(9):1450–7. https://doi.org/10.1016/j.jand.2016.04.004.
9. Shi Y, Davies A, Allman-Farinelli M. The association between food insecurity and dietary outcomes in university students: a systematic review. *J Acad Nutr Diet* 2021;**121**(12):2475–2500.e1. https://doi.org/10.1016/j.jand.2021.07.015. Dec.
10. Farahbakhsh J, Hanbazaza M, Ball GDC, Farmer AP, Maximova K, Willows ND. Food insecure student clients of a university-based food bank have compromised health, dietary intake and academic quality. *Nutr Diet. Feb* 2017;**74**(1):67–73. https://doi.org/10.1111/1747-0080.12307.
11. Hall RP, Ranganathan S, Agnew J, Christie ME, Clark S, Kirk G, et al. Virginia tech food access and security study. *Virginia Tech* 2019:18–20. http://hdl.handle.net/10919/95218.
12. Martinez SM, Grandner MA, Nazmi A, Canedo ER, Ritchie LD. Pathways from food insecurity to health outcomes among California university students. *Nutrients* 2019;**11**(6). https://doi.org/10.3390/nu11061419. Jun 24.
13. Mei J, Fulay AP, Wolfson JA, Leung CW. Food insecurity and dietary intake among college students with unlimited meal plans at a large, Midwestern university. *J Acad Nutr Diet. Nov* 2021;**121**(11):2267–74. https://doi.org/10.1016/j.jand.2021.04.009.
14. Mirabitur E, Peterson KE, Rathz C, Matlen S, Kasper N. Predictors of college-student food security and fruit and vegetable intake differ by housing type. *J Am Coll Health* 2016;**64**(7):555–64. https://doi.org/10.1080/07448481.2016.1192543. Oct.
15. Becerra MB, Becerra BJ. Psychological distress among college students: role of food insecurity and other social determinants of mental health. *Int J Environ Res Publ Health* 2020;**17**(11). https://doi.org/10.3390/ijerph17114118. Jun 9.
16. Martinez SM, Frongillo EA, Leung C, Ritchie L. No food for thought: food insecurity is related to poor mental health and lower academic performance among students in California's public university system. *J Health Psychol* 2020;**25**(12):1930–9. https://doi.org/10.1177/1359105318783028. Oct.
17. Raskind IG, Haardörfer R, Berg CJ. Food insecurity, psychosocial health and academic performance among college and university students in Georgia, USA. *Public Health Nutr* 2019;**22**(3):476–85. https://doi.org/10.1017/s1368980018003439. Mar.
18. Coffino JA, Spoor SP, Drach RD, Hormes JM. Food insecurity among graduate students: prevalence and association with depression, anxiety and stress. *Publ Health Nutr* 2021;**24**(7):1889–94. https://doi.org/10.1017/s1368980020002001. May.
19. Mahmoud JS, Staten R, Hall LA, Lennie TA. The relationship among young adult college students' depression, anxiety, stress, demographics, life satisfaction, and coping styles. *Issues Ment Health Nurs* 2012;**33**(3):149–56. https://doi.org/10.3109/01612840.2011.632708. Mar.
20. Soet J, Sevig T. Mental health issues facing a diverse sample of college students: results from the college student mental health Survey. *NASPA J* 2006/10/01 2006;**43**(3):410–31. https://doi.org/10.2202/1949-6605.1676.

21. Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. *J Health Soc Behav* 1983;**24**(4):385–96. https://doi.org/10.2307/2136404.
22. Diener E, Wirtz D, Tov W, Kim-Prieto C, Choi D, Oishi S, et al. New well-being measures: short scales to assess flourishing and positive and negative feelings. *Soc Indicat Res* 2010;**97**:143–56. https://doi.org/10.1007/s11205-009-9493-y.
23. Kansky J, Diener E. Benefits of well-being: health, social relationships, work, and resilience. *J Positive Psychology Wellbeing* 2017;**1**(2):129–69.
24. Diener E, Diener C, Choi H, Oishi S. Revisiting "most people are happy"—and discovering when they are not. *Perspect Psychol Sci* 2018;**13**(2):166–70. https://doi.org/10.1177/1745691618765111.
25. U.S. Department of Agriculture. *U.S. Household Food Security Survey Module: Six-Item Short Form Economic Research Service* 2012;**2022**(June 15). https://www.ers.usda.gov/media/8282/short2012.pdf.
26. Shrout PE, Bolger N. Mediation in experimental and nonexperimental studies: new procedures and recommendations. *Psychol Methods* 2002;**7**(4):422–45. Dec.
27. Myers CA, Mire EF, Katzmarzyk PT. Trends in adiposity and food insecurity among US adults. *JAMA Netw Open* 2020;**3**(8):e2012767. https://doi.org/10.1001/jamanetworkopen.2020.12767. Aug 3.
28. Huelskamp A, Waity J, Russell J. Effects of campus food insecurity on obesogenic behaviors in college students. *J Am Coll Health* 2021;**69**(5):572–5. https://doi.org/10.1080/07448481.2019.1684298. Jul.
29. Greene ML, Way N, Pahl K. Trajectories of perceived adult and peer discrimination among Black, Latino, and Asian American adolescents: patterns and psychological correlates. *Dev Psychol* 2006;**42**:218–36. https://doi.org/10.1037/0012-1649.42.2.218.
30. Okazaki S. Impact of racism on ethnic minority mental health. *Perspect Psychol Sci* 2009;**4**(1):103–7. https://doi.org/10.1111/j.1745-6924.2009.01099.x.
31. Oliver 2nd MD, Datta S, Baldwin DR. Wellness among African-American and Caucasian students attending a predominantly White institution. *J Health Psychol* 2019;**24**(12):1637–45. https://doi.org/10.1177/1359105317694484. Oct.
32. Wright JI, Whyne EZ, Lehrer HM, Woo J, Steinhardt MA. The roles of resilience and belonging in mediating the association between positivity and anxiety among underrepresented college students. *J Am Coll Health* 2022;**70**(8):2311–7. https://doi.org/10.1080/07448481.2020.1851235. Nov-Dec.
33. Brown DL. African American resiliency: examining racial socialization and social support as protective factors. *J Black Psychol* 2008;**34**(1):32–48. https://doi.org/10.1177/0095798407310538.
34. Frazier P, Gabriel A, Merians A, Lust K. Understanding stress as an impediment to academic performance. *J Am Coll Health* 2019;**67**(6):562–70. https://doi.org/10.1080/07448481.2018.1499649. Aug-Sep.
35. Peterson N, Freidus A, Tereshenko D. Why college students don't access resources for food insecurity: stigma and perceptions of need. *Annals of Anthropological Practice* 2022;**46**(2):140–54. https://doi.org/10.1111/napa.12190.
36. DeBate R, Himmelgreen D, Gupton J, Heuer JN. Food insecurity, well-being, and academic success among college students: implications for post COVID-19 pandemic programming. *Ecol Food Nutr* 2021;**60**(5):564–79. https://doi.org/10.1080/03670244.2021.1954511. 2021/09/03.
37. Yau YH, Potenza MN. Stress and eating behaviors. *Minerva Endocrinol. Sep* 2013;**38**(3):255–67.
38. Nikolaus CJ, Ellison B, Nickols-Richardson SM. College students' interpretations of food security questions: results from cognitive interviews. *BMC Publ Health* 2019;**19**(1):1282. https://doi.org/10.1186/s12889-019-7629-9. Oct 11.
39. Anderson A, Lazarus J, Anderson Steeves E. Navigating hidden hunger: an exploratory analysis of the lived experience of food insecurity among college students. *Int J Environ Res Publ Health* 2022;(19):19. https://doi.org/10.3390/ijerph191912952. Oct 10.
40. Richards R, Stokes N, Banna J, Cluskey M, Bergen M, Thomas V, et al. A comparison of experiences with factors related to food insecurity between college students who are food secure and food insecure: a qualitative study. *J Acad Nutr Diet. Mar* 2023;**123**(3):438–453 e2. https://doi.org/10.1016/j.jand.2022.08.001.
41. Esaryk EE, Moffat LF, Ritchie LD, Martinez SM. Helping college students get supplemental nutrition assistance program: facilitators of and barriers to students accessing the federal nutrition assistance program. *J Nutr Educ Behav. May* 2022;**54**(5):422–31. https://doi.org/10.1016/j.jneb.2022.02.008.
42. Freudenberg N, Goldrick-Rab S, Poppendieck J. College students and SNAP: the new face of food insecurity in the United States. *Am J Publ Health* 2019;**109**(12):1652–8. https://doi.org/10.2105/AJPH.2019.305332. Dec.
43. Watts A, Araiza AL, Fernandez CR, Rosenthal L, Vargas-Rodriguez I, Duroseau N, et al. The campaign for universal free lunch in New York city: lessons learned. *Pediatrics* 2021;**148**(4). https://doi.org/10.1542/peds.2020-049734. Oct.
44. Holford A, Rabe B. Going universal. The impact of free school lunches on child body weight outcomes. *J Publ Econ* 2022;**3**:100016. https://doi.org/10.1016/j.pubecp.2022.100016. 2022/01/01/.
45. Schwartz AE, Rothbart MW. Let them eat lunch: the impact of universal free meals on student performance. *J Pol Anal Manag* 2020;**39**(2):376–410. https://doi.org/10.1002/pam.22175.
46. Cohen JFW, Hecht AA, McLoughlin GM, Turner L, Schwartz MB. Universal school meals and associations with student participation, attendance, academic performance, diet quality, food security, and body Mass Index: a systematic review. *Nutrients* 2021;**13**(3):911.
47. van Woerden I, Hruschka D, Vega-Lomicronpez S, Schaefer DR, Adams M, Bruening M. Food insecure college students and objective measurements of their unused meal plans. *Nutrients* 2019;**11**(4). https://doi.org/10.3390/nu11040904. Apr 23.

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Original Research

Gambling helpline contacts during COVID-19-related availability restrictions: an interrupted time series analysis

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ABSTRACT

Objectives: Gambling causes significant public health harms that are addressed in the help service network. Helplines are the most widely used service among those experiencing harms. The COVID-19 pandemic changed the global gambling landscape. This study assesses the effect of COVID-19-related restrictions on help-seeking for gambling via helplines.
Study design: We analysed data of national helplines in Sweden, Finland, and Denmark before and during the pandemic. The countries differed in their restrictions on the availability and accessibility of gambling during the pandemic.
Methods: We performed an interrupted time series analysis of contact and web traffic data to helplines in Sweden, Finland, and Denmark before and during the COVID-19 pandemic (2017–2021). We also compared forecasted time series to the actual data to assess change.
Results: The results show diverging patterns across the three countries. In Sweden, the number of helpline contacts remained stable throughout COVID-19, but there was an increasing trend in website visits. In Finland, the number of contacts declined during the first wave but rebounded during the second wave. Website visitation increased moderately. In Denmark, the number of contacts to the helpline soared over the COVID-19 period.
Conclusions: The diverging results suggest that help-seeking behaviour is likely to be impacted by differing policy approaches to gambling availability and limit-setting, visibility of helplines, and the prevalence of different forms of gambling in the three Nordic countries before and during the pandemic. This has implications for a preventive public health approach for gambling.

Introduction

Gambling causes serious harms to individuals, concerned significant others (CSOs), and societies. Globally, the prevalence rates of self-reported problem gambling range between about .5 and 7.6 percent in the population, with an average rate of about 2.3 percent.[1,2] Prevalence rates vary according to context but also depending on methodological differences such as measures and samples.[1] In addition to problematic behaviour, gambling also causes a variety of other harms, ranging from financial difficulties and relationship harms to mental health problems and even suicidality.[3–5] Some gambling products cause more harms and problems than others. A meta-analysis of problem gambling risk factors[6] shows that the highest odds ratios (ORs) are for online gambling (OR 7.59), non-casino electronic gambling machine (EGM) gambling (OR 7.20), and casino EGM gambling (OR 6.78). Greater availability has also been connected to increased problems or harms, although levels of problem gambling may plateau over time due to 'adaptation' or more effective harm prevention.[7,8]

After onset, gambling problems are addressed by help, support, and treatment services. Financial and emotional issues have been identified as the main motives for help seeking.[9] Most help services are aimed at individuals who experience severe harms due to their own gambling. Services include formal approaches such as social work, medical help, peer support, and debt counselling but also informal approaches such as self-help.[10–12] Overall, a minority of

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individuals with gambling-related problems seek help. A recent systematic review suggested that only four percent of individuals with moderate problems and 20 percent of individuals with severe problems sought help.[13]

Helplines are a first-line support for individuals experiencing problems with gambling.[14–16] A recent survey found that 82 gambling helplines operate globally.[14] Helplines offer brief interventions, motivational interviewing, emotional support, information, and referrals to other treatment.[14,17] Helplines provide services via telephone, but in many cases also via chats, e-mail, text messages, as well as online resources.[14] Helplines are also actively promoted, and individuals experiencing gambling problems are usually aware of them.[16]

Many helplines routinely collect data on contacts. Data consist either of pre-set questionnaires or spontaneous observations by employees.[14] Statistical data from helplines have been used to inform research about developments in the gambling field, including gambling products that cause problems,[18,19] the socio-demographic characteristics of help-seekers,[20–22] the types of harms experienced,[23] and education.[24] Helpline data can therefore be useful in measuring trends and changes in problematic gambling within and across societies.

In 2020, the onset of the COVID-19 pandemic caused significant changes in the field of gambling. Across jurisdictions, availability was restricted due to lockdown measures. Regulatory actions were also taken in some jurisdictions to curb possible increases in online gambling. These included stricter limit-setting measures as well as marketing restrictions.[25] Evidence on the impacts of the pandemic on gambling suggests an overall reduction in gambling behaviour in most contexts, with no significant substitution from land-based to online gambling.[26–28] Data from treatment providers have also not indicated increases in treatment uptake during COVID-19.[29,16] Available qualitative and quantitative evidence suggests that the reduced availability of gambling during the pandemic may have translated to reduced service needs.[16,30,31]

However, little research has been conducted on the effects of COVID-19 and related restrictions on availability and gambling opportunities using helpline data. Helpline data is a comparatively reliable data source to investigate changes during COVID-19 because unlike many other treatment services for gambling problems, helplines remained operational during the pandemic.[31] Only one study from Ontario[16] used gambling helpline data from a 5-year period (March 2015–March 2021) and interrupted time series analyses to examine how changes in gambling availability due to COVID-19 was visible in helpline calls. The study showed an initial dramatic decline in contacts after casino closures in 2020, but a later rebound. No comparative evidence currently exists on the effects of COVID-19 on helpline contacts.

The aim of the current study is to examine the impact of COVID-19 restrictions on contacts to gambling helplines in three Nordic countries (Sweden, Finland, and Denmark) with differing approaches to limiting gambling availability during the pandemic. Using longitudinal data (2017–2021) from helplines and a comparative setting allows wider conclusions on the differences between the impact of restrictions during COVID-19, but also gambling policy systems, availability, and effective prevention of harm.

Methods

Context

Sweden, Finland, and Denmark have similar gambling markets with wide availability of different types of gambling both land-based and online. In Sweden and Denmark, online gambling is provided by licensed operators, whereas in Finland, online gambling is provided by a national monopoly operator. Online gambling is prevalent in each country. Each included country also has a national helpline to assist with gambling-related problems.

The Swedish Stödlinjen helpline is run by the Centre for Psychiatry Research at Stockholm County Council and funded by the Swedish Ministry of Health and Social Affairs. Stödlinjen was established in 1999. It provides support to gamblers and CSOs. Stödlinjen provides service by phone, chat, e-mail, and online resources such as self-testing. The helpline operates on weekdays between 9 am and 4 pm (except Mondays between 9 am and 9 pm and Thursdays between 11 am and 9 pm).

Peluuri is a Finnish gambling help service. It was established in 2004, and it has been financed by the monopolistic gambling operator Veikkaus. The target group of the services of Peluuri are gamblers, CSOs, and other professionals encountering gambling harms. The service also welcomes digital gamers and their significant others. The helpline operates on weekdays between 12am and 6pm via phone and chat. In addition, Peluuri provides online resources, including online peer support.

StopSpillet is the Danish national gambling helpline. StopSpillet was established in 2019 as the first national gambling helpline service, and it is run by the Danish Gambling Authority. The main target groups are gamblers, CSOs, and professionals. StopSpillet also caters for digital gamers and their CSOs. StopSpillet operates via telephone and chat. The telephone services operate during weekdays between 9 am and 9 pm (except Fridays between 9 am and 5 pm). The chat operates from Monday to Thursday between 5 pm and 9 pm.

Data

We used two separate data sets collected in the daily operations of Stödlinjen (SE), Peluuri (FI), and StopSpillet (DK).

The first data set consists of helplines' counselling services (telephone and chat). In each country, contacts are logged into the helpline system automatically or manually. The collected variables differ across helplines, but the data entry procedure is similar: after the call, the counsellor manually enters data about the content of the conversation using an online interface, while the time stamps of calls are automatically logged.

For this study, we focused only on the number of calls, and not their contents. We included all calls or other contacts that had a start and end time, regardless of if the contacts were from gamblers, CSOs, or other types of callers (e.g. from treatment providers or wrong numbers). The wrong numbers mainly consisted of contact attempts to gambling providers. However, these were included because they also provide a possibility for an intervention. The Swedish helpline provided counselling service data for the period 2017 to 2020, the Finnish helpline for the period 2017 to 2021, and the Danish helpline for the period 2019 to 2021 (the Danish helpline started their operations in 2019).

The second data source consists of the number of visitors to helpline websites. In each country, data were collected using Google analytics from 2019 to 2021. In Sweden and Finland, Google analytics data were available daily. In the Danish case, only monthly Google analytics data were available, with a shorter baseline (three months). For this reason, we did not perform a forecast and present only actual data for Denmark.

COVID-19 restrictions

The most important periods of societal restrictions and availability limitations of gambling during COVID-19 were identified based on online scanning of Swedish, Finnish, and Danish governmental websites, websites of gambling operators in these

Table 1
Restrictions on gambling availability during COVID-19 in Sweden, Finland, and Denmark.

Restriction	Sweden	Finland	Denmark
Closure of EGMs, casinos, arcades			
First wave	30.3.2020–5.7.2021[a]	14.3.2020–15.7.2020	18.3.2020–7.6.2020
Second wave	–	26.11.2020–6.5.2021[c]	9.12.2020–20.5.2021
Third wave	–	6.8.2021–1.10.2021[c]	17.12.2021–31.1.2022
Reduced limits for online gambling	30.6.2020–14.11.2021	1.5.2020–18.6.2021	n/a
Sport event cancellations[b]	13.3.2020–15.6.2020		

[a] The four land-based casinos in Sweden were closed at the casino's own initiative due to visitor restrictions.
[b] Major European football leagues (England, Germany, Italy, Spain, France + Sweden, Finland, Denmark) and major hockey leagues (NHL, KHL + Sweden, Finland). Games cancelled on average on the 13th of March 2020. Games resumed at varying times but starting around the week of 15th of June 2020.
[c] Varying regional restrictions, not applicable to the whole country simultaneously.

countries, and information channels of popular sports leagues in the Nordics and Europe. Table 1 summarises the main periods of restrictions used in the interrupted time series analysis.

Analysis

We analysed the influence of COVID-19-related restrictions on help-seeking using interrupted time series analysis. The method allows analysing how events in society (the COVID-19 pandemic) affect subsequent behaviours (help-seeking via gambling helplines).[32]

We analysed both sets of data using dynamic harmonic regression models with ARIMA errors, using the R-packages fable and feasts.[33,34] These models are feasible when a time series contains complex seasonality, as suggested by Hyndman and Athanasopoulos.[35] The number of Fourier terms for each seasonal component were selected based on ocular inspection.[35] To prevent holiday effects in the counselling service data, we calculated the average number of calls per day and week. Based on this, if a helpline operated only three days instead of five, the average number of calls per day were based on a three-day week. This *modus operandi* is suggested by Hyndman and Athanasopoulos[35] to prevent arbitrary patterns in the time series. The Google analytics data on the number of visitors to helpline webpages were analysed as daily data without holiday adjustments, since webpages are available at any time of day and regardless of holidays.

We modelled counselling contacts by adding monthly and yearly seasonal components to the models and presuming that a ‘helpline week’ is five days. The monthly period was therefore set to 4.35 (a month contains 4.35 weeks on average), and the yearly period was, in the same manner, set to 52.2. For the Google analytics data, three seasonal components were added to the models: weekly, monthly, and yearly. To determine if the residuals were ‘white noise’, we performed Box–Pierce tests. Moreover, and to minimise bias, if the residual's mean differed from zero, the residual mean was subtracted from the forecasted point estimates as suggested by Hyndman and Athanasolous.[35] The forecasted time series were then compared to actual data by calculating prediction errors for each period of interest. The prediction errors are presented in percent with *P*-values and 95% confidence intervals.

The data were forecasted for the period 13.3.2020 to 13.3.2021, except for Sweden where the period ended on 31.12.2020. For all data sets, comparison between predicted and actual data were made for the periods; 1) during cancelled sports events, 2) the first wave of the pandemic, 3) reduced deposit limits (Sweden and Finland), 4) between the first and second wave of the pandemic, 5) the second wave of the pandemic, and 6) the entire forecast period.

Table 2
Difference (%) between actual and forecasted data for Sweden, Finland, and Denmark.

Country	Source	Period	Diff %	95% CI	*P*-value
Sweden	**Web**	**13.3–15.6 2020**[a,b]	**12.7**	**9.2, 16.1**	**<.0001**
Sweden	Web	30.6–31.12 2020[c]	.5	−2.1, 3.1	.68
Sweden	**Web**	**13.3–31.12 2020**[f]	**5.3**	**3.1, 7.4**	**<.0001**
Sweden	Telephone	W11–W25 2020[a,b]	−1.1	−12.1, 9.9	.83
Sweden	Telephone	W27–W52 2020[c]	.1	−5.9, 7.6	.80
Sweden	Telephone	W11–W52 2020[f]	.4	−5.0, 5.8	.88
Finland	Web	13.3–15.7 2020[a,b]	2.9	−1.8, 7.6	.23
Finland	Web	16.7–8.12 2020[d]	1.3	−1.7, 4.4	.39
Finland	**Web**	**26.11.20–13.3.21**[e]	**5.5**	**1.3, 9.7**	**.010**
Finland	**Web**	**13.3.20–13.3–21**[c,f]	**4.0**	**1.7, 6.4**	**<.001**
Finland	**Telephone**	**W11–W29 2020**[a,b]	**−15.8**	**−26.4, -5.1**	**<.01**
Finland	Telephone	W30–W47 2020[d]	−10.6	−20.4, .26	.055
Finland	**Telephone**	**W48 2020-W10 2021**[c]	**12.5**	**1.1, 24.0**	**.033**
Finland	Telephone	W11 2020-W10 2021[c,f]	−2.6	−10.2, 5.1	.50
Denmark	**Telephone**	**W11–W25 2020**[a,b]	**38.2**	**4.7, 71.2**	**<.01**
Denmark	Telephone	W26–W49 2020[d]	−.4	−16.0, 15.1	.95
Denmark	**Telephone**	**W50 2020-W10 2021**[e]	**105.8**	**81.1130.5**	**<.0001**
Denmark	**Telephone**	**W11 2020-W10 2021**[f]	**37.9**	**20.2, 55.6**	**<.001**

Bolded lines indicate *P*-values of 0.05 or less.
[a] Cancelled sports events.
[b] The first wave of the pandemic.
[c] Reduced deposit limits (Sweden and Finland).
[d] Between the first and second wave.
[e] The second wave of the pandemic.
[f] The entire period.

The code and data used for the analysis are available in a separate repository https://osf.io/gk42s/.

Results

Result show that Sweden, Finland, and Denmark differ in terms of how the COVID-19-related restrictions affected contacts to helplines. Table 2 and Fig. 1 show the difference in percentage between actual and forecasted data (contacts and Google analytics). Regarding regression model diagnostics, the Box–Pierce tests showed non-significant results, indicating that the residuals in all models can be considered 'white noise'.

In Sweden, we found no support for any effect on helpline counselling contacts of the various COVID-19 restrictions on gambling availability (closures of land-based casinos), cancelled sports events, or the temporary deposit limits for online gambling. However, there was a general increase in website visitors, 5.3 percent for the entire period, and a 12.7 percent increase during the period of cancelled sports events.

In Finland, counselling contacts decreased by 15.8 percent during the initial phase of the pandemic (first wave), during which there were restrictions on both land-based and online gambling. However, during the second wave of closures, counselling contacts increased by 12.5 percent. In terms of website visitors in Finland, the number of visitors increased by four percent over the first year of the pandemic.

Denmark showed a different pattern compared to Sweden and Finland. Counselling contacts increased dramatically during the first and second waves of reduced gambling opportunities, by 38.2 percent and 105.8 percent, respectively. This was observed even though many land-based gambling opportunities were closed in Denmark.

Discussion

This paper has investigated changes and trends in help-seeking for gambling-related problems during COVID-19-related restrictions in Sweden, Finland, and Denmark, using longitudinal statistical data collected by national helplines for gambling. The

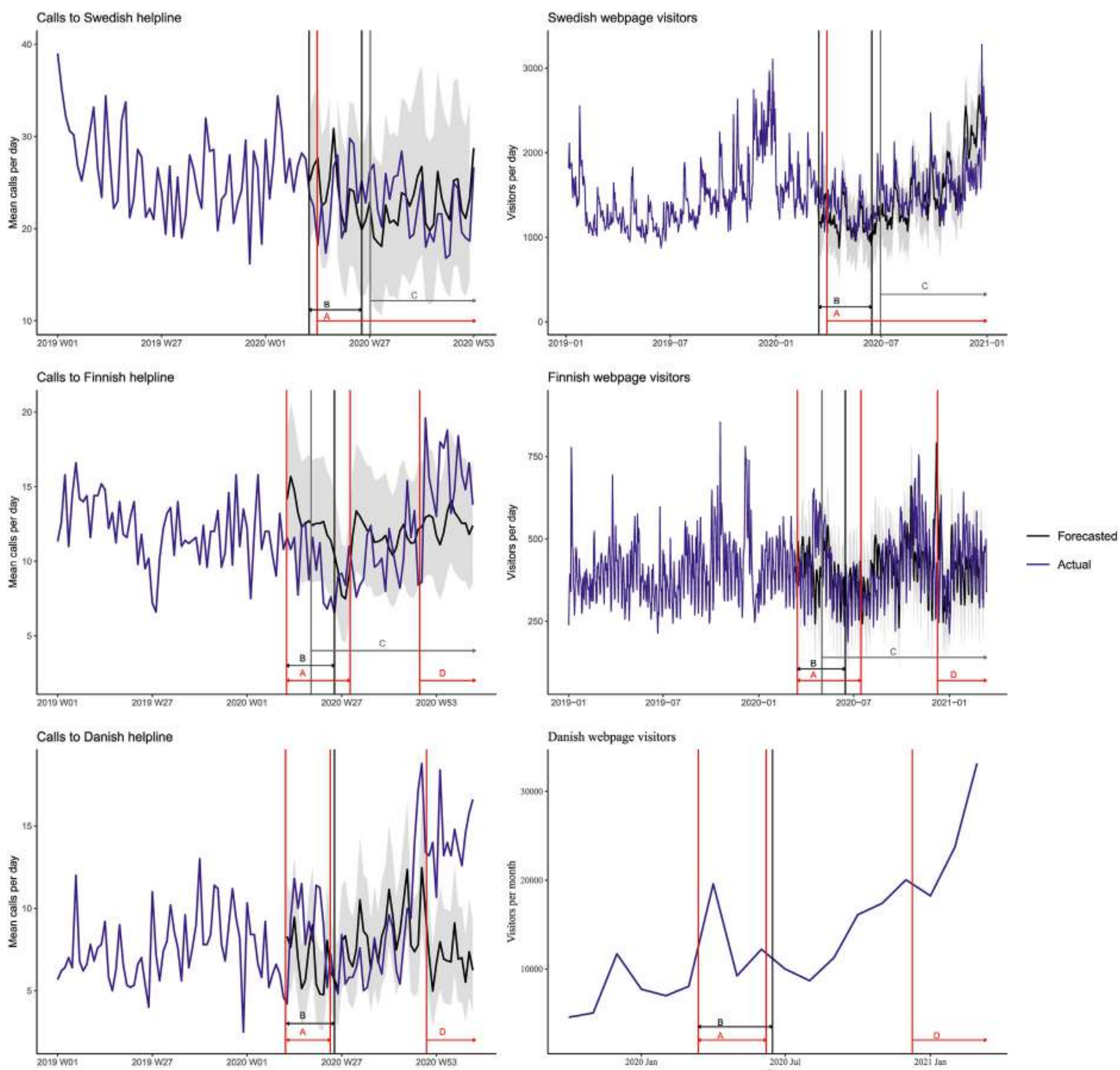

Fig. 1. Time series with forecasted data (with 95% prediction intervals) and actual data for Sweden, Finland, and Denmark. The various COVID-19 restrictions are marked with vertical lines. Note. A = restriction of land-based gambling opportunities during the first wave of the pandemic, B = cancellation of sports events, C = mandatory deposit limits, D = restriction of land-based gambling opportunities during the second wave of the pandemic.

results have shown diverging patterns in terms of the number of contacts. In Sweden, the number of helpline contacts has remained stable, and COVID-19 does not appear to have affected help-seeking behaviour. In Finland, the number of contacts initially declined but later rebounded, whereas in Denmark, the number of helpline contacts soared during the entire period. This divergence can be explained by the baseline prevalence of different gambling forms, the visibility of helplines, and different policy approaches to gambling availability and limit-setting.

First, the results show that COVID-19-related restrictions did not impact all contexts similarly. Previous literature on the effects of the pandemic on gambling has suggested that, in most cases, online gambling did not substitute land-based provision. Instead, land-based gambling participation reduced following restrictions, whereas online gambling intensified among some of those who already gambled online.[26–28,36] The baseline prevalence of online gambling, and particularly the role of online gambling as a vector for harms and help-seeking before the pandemic, may explain part of the divergence. In Finland, a wide availability of land-based EGMs in non-casino environments had translated into high levels of EGM harms and help-seeking for EGM harms before the pandemic.[37,38] Unlike in most contexts, in prepandemic Finland, online gambling was not connected to higher gambling harms than land-based gambling due to harms caused by EGMs.[39] The closure of land-based EGMs is likely to be behind reduced help-seeking in the Finnish context. In Denmark and Sweden, online forms of gambling were more important causes of harms before the pandemic.[40,41] Previous evidence from Sweden and Denmark also suggests that online gambling did not decrease significantly in these contexts during the first months of the pandemic.[42,36,43,44] This can explain why closures of land-based gambling opportunities did not translate to similar reductions in help-seeking in Sweden and Denmark.

Second, the results suggest that advertising and visibility of helplines attracts traffic to these services. In each country, licensed or monopolistic gambling companies must advertise helplines. This visibility can drive particularly website visitation. In Denmark, a public information campaign advertising the services for StopSpillet occurred during spring and autumn of 2020 (March 9–April 19; September 14–October 25) in social media as well as outdoors and in cinemas. StopSpillet is also younger than its Swedish and Finnish counterparts, which may partly explain the increase in help-seeking in Denmark. On the other hand, unlicensed online providers do not advertise helplines. Particularly in Finland, with a monopolistic gambling market, a significant part of gambling, and particularly problematic gambling, takes place in non-licensed online websites. In 2021, the market share of the monopoly was only 59 percent in the digital channel (estimation of H2 gambling capital, cited by Veikkaus).[45] This channelling rate is notably lower than in the licensed markets of Sweden and Denmark (closer to 90 percent in both contexts). This may also partly explain the lower numbers of help-seeking in Finland.

Third, restrictions on mandatory gambling spending and deposit limits may reduce overall harms and problems. Sweden and Finland lowered the mandatory loss limits for online gambling during 2020, whereas Denmark did not. Previous research on mandatory limit-setting suggests that most players appear to stop gambling when reaching their limits. Reaching limits is also more common among high intensity gamblers.[46] However, particularly in Sweden, the mandatory deposit limit was relatively high even at the lowered level (5000 SEK, or about 500 euros a week per operator, compared to 500 euros a month for the monopoly operator in Finland). Furthermore, the possibility to gamble on unlicensed websites may have reduced the impact of mandatory limits in both countries.[47,37] It is therefore likely that the lowered limits were rather insignificant, particularly in Sweden.

The current study has been limited to three Nordic countries. The results are therefore not necessarily generalisable to other contexts. The study has also been limited by issues related to data comparability and availability. Data from the three helplines were comparable on a limited set of call frequency variables due to country-specific registration practices. The granularity of web traffic data also limited comparative time series analyses across the three countries. Data collection should, of course, not be the main priority of helplines, but more unified practices across helplines in how data are collected and reported would be useful for further research efforts.

This study has nevertheless shown that helpline data can be a valuable source for research on gambling harms and problems, as well as their evolution within and across contexts. To advance knowledge on the precipitators of help-seeking, it is also necessary to conduct qualitative analyses on the content of helpline contacts, and particularly regarding the types of gambling products that callers identify as causing harm. The results of the current study have also shown that different policy approaches affect help-seeking. Particularly reduced availability, low mandatory limits, as well as visibility of available help resources can be effective in reducing gambling harms and the burden of gambling on public health.

Author statements

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Ethical approval

The study was conducted in accordance with the Helsinki Declaration and was approved by the Swedish Ethical Review Authority (decision number 2022-03651-01), the vice dean at the Faculty of Social Science and Humanities at Aalborg University, and by the University of Helsinki Ethical Review Board in Humanities and Social and Behavioural Sciences (decision number 56/2022).

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Competing interests

HW, VM, and SK have no competing interests to report. DF has received grants from Svenska Spel's research council for projects on concerned significant others and e-sportbetting. OM has received grants from Svenska Spel's independent research council for projects on internet-delivered treatments for gambling disorder and psychiatric comorbidities.

References

[1]. Williams R, Volberg R, Stevens R. *The population prevalence of problem gambling: methodological influences, standardized rates, jurisdictional differences, and worldwide trends*. Ontario Problem Gambling Research Centre; 2012.

[2]. Calado F, Griffiths M. Problem gambling worldwide: an update and systematic review of empirical research (2000–2015). *J Behav Addict* 2016;**5**: 592–613. https://doi.org/10.1556/2006.5.2016.073.
[3]. Marionneau V, Egerer M, Raisamo S. Frameworks of gambling harms: a comparative review and synthesis. *Addict Res Theory* 2022:1–8. https://doi.org/10.1080/16066359.2022.2113071.
[4]. Wardle H, Reith G, Langham E, Rogers RD. Gambling and public health: we need policy action to prevent harm. *BMJ* 2019;**365**:l1807. https://doi.org/10.1136/bmj.l1807.
[5]. Langham E, Thorne H, Browne M, Donaldson P, Rose J, Rockloff M. Understanding gambling related harm: a proposed definition, conceptual framework, and taxonomy of harms. *BMC Publ Health* 2016;**16**:1–23. https://doi.org/10.1186/s12889-016-2747-0.
[6]. Allami Y, Hodgins DC, Young M, Brunelle N, Currie S, Dufour M, et al. A meta-analysis of problem gambling risk factors in the general adult population. *Addiction* 2021;**116**:2968–77. https://doi.org/10.1111/add.15449.
[7]. Storer J, Abbott M, Stubbs J. Access or adaptation? A meta-analysis of surveys of problem gambling prevalence in Australia and New Zealand with respect to concentration of electronic gaming machines. *Int Gambl Stud* 2009;**9**: 225–44. https://doi.org/10.1080/14459790903257981.
[8]. Abbott M. The changing epidemiology of gambling disorder and gambling-related harm: public health implications. *Publ Health* 2020;**184**:41–5. https://doi.org/10.1016/j.puhe.2020.04.003.
[9]. Loy J, Grüne B, Braun B, Samuelsson E, Kraus L. Help-seeking behaviour of problem gamblers: a narrative review. *Sucht* 2019;**64**:259–72. https://doi.org/10.1024/0939-5911/a000560.
[10]. Johnstone P, Regan M. Gambling harm is everybody's business: a public health approach and call to action. *Publ Health* 2020;**184**:63–6. https://doi.org/10.1016/j.puhe.2020.06.010.
[11]. Manning V, Dowling N, Rodda S, Cheetham A, Lubman D. An examination of clinician responses to problem gambling in community mental health services. *J Clin Med* 2020;**9**:2075. https://doi.org/10.3390/jcm9072075.
[12]. Hing N, Russell A, Gainsbury S, Blaszczynski A. Characteristics and help-seeking behaviors of Internet gamblers based on most problematic mode of gambling. *J Med Internet Res* 2015;**17**:e3781. https://doi.org/10.2196/jmir.3781.
[13]. Bijker R, Booth N, Merkouris S, Dowling N, Rodda S. Global prevalence of help-seeking for problem gambling: a systematic review and meta-analysis. *Addiction* 2022;**117**:2972–85. https://doi.org/10.1111/add.15952.
[14]. Berman A, Arillo A, Berntsson A, Rodda S. Helplines for problem gambling worldwide: what do they do and whom do they reach? *J Gambl Issues* 2023.
[15]. Darbeda S, Aubin H, Lejoyeux M, Luquiens A. Characteristics of gamblers who use the French national problem gambling helpline and real-time chat facility: longitudinal observational study. *JMIR Forma Res* 2020;**4**:20. https://doi.org/10.2196/13388.
[16]. Turner N, Cook S, van der Maas M. The impact of Covid-19 on gambling-related crises calls in Ontario, Canada: an interrupted time series analysis. *J Gambl Issues* 2022;**50**:185–202.
[17]. Ledgerwood D, Arfken C, Wiedemann A, Bates K, Holmes D, Jones L. Who goes to treatment? Predictors of treatment initiation among gambling help-line callers. *Am J Addict* 2013;**22**:33–8. https://doi.org/10.1111/j.1521-0391.2013.00323.x.
[18]. Abbott M. Gambling and gambling harm in New Zealand: a 28-year case study. *Int J Ment Health Ad* 2017;**15**:1221–41. https://doi.org/10.1007/s11469-017-9767-6.
[19]. Rossow I, Hansen M. Gambling and gambling policy in Norway: an exceptional case. *Addiction* 2016;**111**:593–8. https://doi.org/10.1111/add.13172.
[20]. Bastiani L, Fea M, Potente R, Luppi C, Lucchini F, Molinaro S. National helpline for problem gambling: a profile of its users' characteristics. *J Addict* 2015: 659731. https://doi.org/10.1155/2015/659731.
[21]. Kim H, Hodgins D, Bellringer M, Abbot M. Gender differences among helpline callers: prospective study of gambling and psychosocial outcomes. *J Gambl Stud* 2016;**32**:605–23. https://doi.org/10.1007/s10899-015-9572-8.
[22]. Potenza M, Steinberg M, Wu R, Rounsaville B, O'Malley S. Characteristics of older adult problem gamblers calling a gambling helpline. *J Gambl Stud* 2006;**22**:241–54. https://doi.org/10.1007/s10899-006-9013-9.
[23]. Luquiens A, von Hammerstein C, Benyamina A, Perney P. Burden and help-seeking behaviors linked to problem gambling and gaming: observational quantitative and qualitative analysis. *JMIR Ment health* 2021;**M8**:e26521. https://doi.org/10.2196/26521.
[24]. Glenn M, Diaz S, Moore L. Using problem gambling helpline data to inform addiction education. *J Teach Addict* 2006;**5**:31–44. https://doi.org/10.1300/J188v05n01_04.
[25]. *Chaire de recherche sur l'étude du jeu Covid-19 et jeux de hasard et d'argent: impacts, transformations et réflexions*. Concordia; 2020.
[26]. Sachdeva V, Sharma S, Sarangi A. Gambling behaviors during Covid-19: a narrative review. *J Addict Dis* 2022;**40**:208–16. https://doi.org/10.1080/10550887.2021.1971942.
[27]. Brodeur M, Audette-Chapdelaine S, Savard AC, Kairouz S. Gambling and the Covid-19 pandemic: a scoping review. *Prog Neuro Psychoph* 2021;**111**: 110389. https://doi.org/10.1016/j.pnpbp.2021.110389.
[28]. Hodgins D, Stevens R. The impact of Covid-19 on gambling and gambling disorder: emerging data. *Curr Opin Psychiatr* 2021;**34**:332. https://doi.org/10.1097/YCO.0000000000000709.
[29]. Håkansson A, Åkeson G, Grudet C, Broman N. No apparent increase in treatment uptake for gambling disorder during ten months of the Covid-19 pandemic: analysis of a regional specialized treatment unit in Sweden. *Int J Env Res Pub He* 2021;**18**:1918. https://doi.org/10.3390/ijerph18041918.
[30]. Donati M, Cabrini S, Capitanucci D, Primi C, Smaniotto R, Avanzi M, et al. Being a gambler during the Covid-19 pandemic: a study with Italian patients and the effects of reduced exposition. *Int J Env Res Pub He* 2021;**18**:424. https://doi.org/10.3390/ijerph18020424.
[31]. Marionneau V, Järvinen-Tassopoulos J. Treatment and help services for gambling during COVID-19: experiences of gamblers and their concerned significant others. *Nordic Stud Alcoh Dr* 2022;**39**:10–24. https://doi.org/10.1177/14550725211030727.
[32]. Schaffer A, Dobbins T, Pearson S. Interrupted time series analysis using autoregressive integrated moving average (ARIMA) models: a guide for evaluating large-scale health interventions. *BMC Med Res Methodol* 2021;**21**. https://doi.org/10.1186/s12874-021-01235-8.
[33]. O'Hara-Wild M, Hyndman R. *Fable: forecasting models for tidy time series (0.3.2)*. 2022.
[34]. O'Hara-Wild M, Hyndman R, Wang E. *Feasts: feature extraction and statistics for time series (03.0)*. 2022.
[35]. Hyndman R, Athanasopoulos G. *Forecasting: principles and practice*. 3rd ed. Melbourne, Australia: OTexts; 2021. OTexts.com/fpp3.
[36]. Månsson V, Wall H, Berman AH, Jayaram-Lindström N, Rosendahl I. A longitudinal study of gambling behaviors during the COVID-19 pandemic in Sweden. *Front Psychol* 2021;**12**:708037.
[37]. Marionneau V, Järvinen-Tassopoulos J. From habit-forming to habit-breaking availability: experiences on electronic gambling machine closures during COVID-19. *Front Psychol* 2022;**12**:6184. https://doi.org/10.3389/fpsyg.2021.788586.
[38]. Peluuri. *Vuosiraportti*. 2019. https://www.peluuri.fi/sites/default/files/2020-10/Peluuri_vuosiraportti_2019_v3_final.pdf.
[39]. Lind K, Marionneau V, Järvinen-Tassopoulos J, Salonen AH. Socio-demographics, gambling participation, gambling settings, and addictive behaviors associated with gambling modes: a population-based study. *J Gambl Stud* 2021:1–16. https://doi.org/10.1007/s10899-021-10074-7.
[40]. Fridberg T, Birkelund J. *Pengespil og spilleproblemer i Danmark 2005–2016*. Copenhagen: The Danish Center for Social Science Research; 2016.
[41]. Wall H, Berman A, Jayaram-Lindström N, Hellner C, Rosendahl I. Gambler clusters and problem gambling severity: a cluster analysis of Swedish gamblers accessing an online problem gambling screener. *Psychol Addict Behav* 2021;**35**:102. https://doi.org/10.1037/adb0000674.
[42]. Lindner P, Forsström D, Jonsson J, Berman AH, Carlbring P. Transitioning between online gambling modalities and decrease in total gambling activity, but no indication of increase in problematic online gambling intensity during the first phase of the COVID-19 outbreak in Sweden: a time series forecast study. *Front Public Health* 2020;**8**:554542.
[43]. Håkansson A. Impact of COVID-19 on online gambling – a general population survey during the pandemic. *Front Psychol* 2020;**11**:568543. https://doi.org/10.3389/fpsyg.2020.568543.
[44]. Håkansson A. Gambling and self-reported changes in gambling during COVID-19 in web survey respondents in Denmark. *Heliyon* 2021;**7**(7).
[45]. Veikkaus. *Vuosi- ja vastuullisuusraportti*. 2021. https://cms.veikkaus.fi/site/binaries/content/assets/dokumentit/vuosikertomus/2021/vuosi_vastuullisuusraportti-2021.pdf.
[46]. Delfabbro P, King D. The value of voluntary vs. mandatory responsible gambling limit-setting systems: a review of the evidence. *Int Gambl Stud* 2021;**21**:255–71. https://doi.org/10.1080/14459795.2020.1853196.
[47]. Håkansson A, Widinghoff C. Gambling despite nationwide self-exclusion: a survey in online gamblers in Sweden. *Front Psychiatr* 2020;**11**:599967. https://doi.org/10.3389/fpsyt.2020.599967.

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Original Research

Impact of socio-economic conditions and perinatal factors on risk of becoming a child looked after: a whole population cohort study using routinely collected data in Wales

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ABSTRACT

Objectives: Between 1997 and 2021, the number of children looked after (CLA) in Wales, UK, increased steadily, with stark inequalities. We aimed to assess how deprivation and maternal and child perinatal characteristics influence the risk of becoming CLA in Wales.
Study design: We constructed a prospective longitudinal cohort of children born in Wales between April 2006 and March 2021 ($n = 395{,}610$) using linked administrative records.
Methods: Survival models examined the risk of CLA from birth by small-area deprivation and maternal and child perinatal characteristics. Population attributable fractions quantify the potential impact of action on modifiable risk factors.
Results: Children from the most deprived fifth of the population were 3.4 times more likely to enter care than those in the least deprived (demographic adjusted hazard ratios [aHRs] 3.40, 95% confidence interval [CI] 3.08, 3.74). Maternal mental health problems in pregnancy (fully aHR, 2.03, 95% CI 1.88, 2.19) and behavioural factors, such as smoking (aHR 2.46, 95% CI 2.34–2.60), alcohol problems (aHR 2.35, 95% CI 1.70–3.23) and substance use in pregnancy (aHR 5.72, 95% CI 5.03–6.51), as well as child congenital anomalies (aHR 1.46, 95% CI 1.16–1.84), low birth weight (aHR 1.28, 95% CI 1.17, 1.39) and preterm birth (aHR 1.16, 95% CI 1.06, 1.26), were associated with higher risk of CLA status. The risk of CLA in the population may be reduced by 35% (95% CI 0.33, 0.38) if children in the two most deprived fifths of the population experienced the conditions of those in the least deprived.
Conclusions: Deprivation and perinatal maternal health are important modifiable risk factors for children becoming CLA. Our analysis provides insight into the mechanisms of intergenerational transfer of disadvantage in a vulnerable section of the child population and identifies targets for public health action.

Introduction

In England and Wales, the number of children looked after (CLA), defined as those in care by order of the State or in care placements (e.g. living with relatives), has risen dramatically over recent years.[1,2] The rates of CLA have increased more in Wales than in England. Between 1997 and 2018, the rates in Wales increased from 49 to 90 per 10,000 children, against a rise of 43–62 per 10,000 in England.[3] There are also stark and rising inequalities in rates of CLA in the United Kingdom. In England, between 2007 and 2019, the greatest increases in CLA rates and CLA entry rates occurred in the most disadvantaged areas.[1,4,5] In Wales, in 2018, 76% of mothers involved in care proceedings lived in the two most deprived fifths.[6]

Reducing the number of children in care is a focus of UK government and policy due to concerns for children's well-being and the high societal costs associated with care entry across the life

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course.[7,8] CLA experience worse educational and employment outcomes, higher mortality rates and higher rates of hospital admissions and criminal justice system involvement.[9,10] Supporting children in receipt of social service intervention and their carers represents a major, long-lasting expenditure at local authority level, and financial pressures are acute in many local authorities in the United Kingdom, hampering investment in the preventative and early years services that may support children at risk of care entry.[11]

Understanding the main drivers of social service intervention across the life course is key to developing strategies to reduce inequalities in CLA rates. Socio-economic disadvantage and family adversity in early childhood are recognised as important risk factors for families' involvement with social care services.[4,6,12–16] The risk factors in the perinatal period, such as young maternal age, lone parenthood, maternal mental health problems, learning difficulty and disability, smoking during pregnancy, and pre- and post-natal substance use, have also been implicated.[17–19] Some studies have shown that individual child perinatal health factors, such as congenital anomalies, low birth weight, and gestational age, are associated with the risk of being taken into care.[20,21] Child's sex was found to be associated with care entry, with males marginally more likely than females to enter care, whilst the impact of ethnicity varies across contexts, with higher rates reported for some ethnic minority groups.[14,22] Family composition, in terms of number of adults and children present in a household, as well as age of children, have also been found to influence the risk of CLA.[13,20,21]

Few studies have assessed the impact of deprivation and a range of maternal and child perinatal factors on risk of CLA in a whole population cohort,[13,15,16,18–21,23,24] none using UK data. In light of this, our study assessed the association between characteristics measured in routine data over the perinatal period until birth, focusing on area-level deprivation, maternal health, and early indicators of child health, and the risk of becoming CLA over a 15-year timespan in Wales. Fig. 1 shows our theoretical model, with the solid-line paths showing the main associations of interest.

Methods

Data sources and study design

We undertook a prospective, observational cohort study of children born in Wales between April 2006 and March 2021, drawing on anonymised, individual-level, population-scale, linked data sources available in the Secure Anonymised Information Linkage (SAIL) databank.[25] Data sources included administrative records from children's social care services, national birth records, population demographics, including residence history, and contact with primary and secondary healthcare services (see Supplementary Material (SM), Table SM2). We report in line with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist (see Supplementary Material (SM), Table SM1).

Because of the overall poor performance of the standard matching process specific to the education and children's social care data sources, additional linkage processing was performed by generating an anonymised version of a child's Unique Pupil Number (UPN).[26] However, only children of school age have a UPN; younger children are typically unlinked. To overcome this limitation, we post-hoc triangulated events in the social care data with corresponding events in other data sources for children with the same week of birth and sex (see Supplementary Material (SM), Section SM2 Record linkage boosting).

Births in Welsh hospitals are comprehensively recorded across three data sources, which we combined to produce a single national birth cohort. We then applied several selection criteria to obtain our analysis sample (Fig. 2). Records were selected if (1) both mother and child had an anonymised linkage field; (2) the birth was recorded as a Welsh live birth with week of birth, sex, gestational age and birth weight recorded; (3) both mother and baby were registered with a SAIL general practice (GP) and recorded as living in Wales; and (4) the mother was aged ≥16 years at birth. Finally, children were excluded from the cohort if they were ever CLA under agreed short-term placements with a local authority, that is,

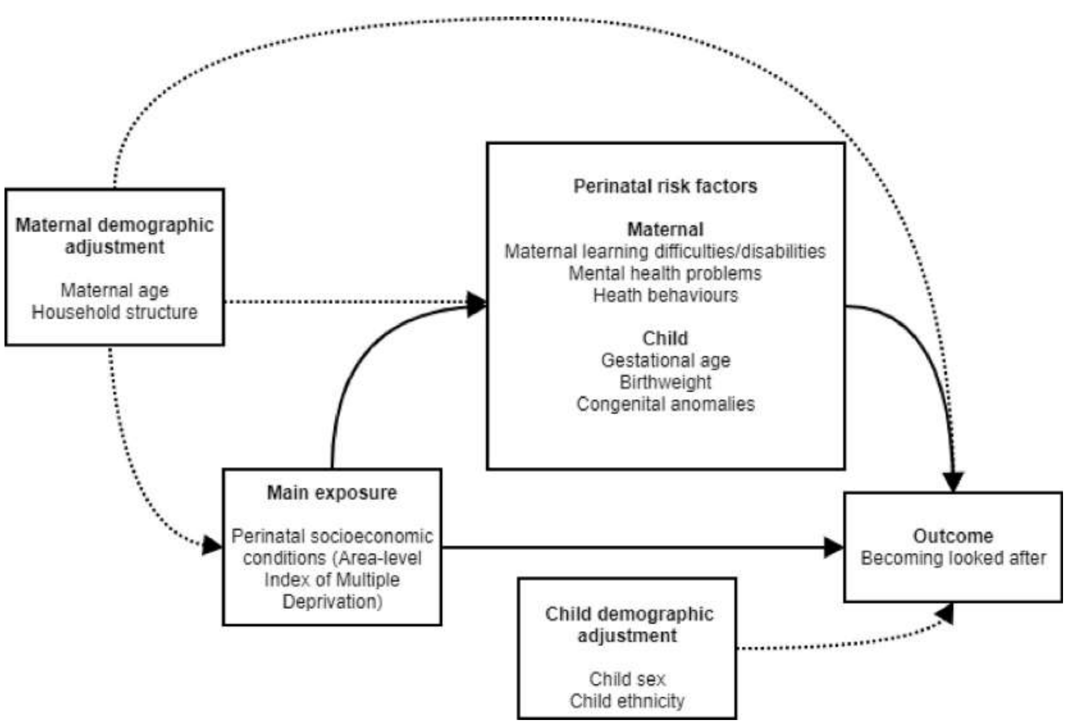

Fig. 1. Diagram of our theoretical model. Plain paths represent the main associations of interest and dotted paths represent adjustment.

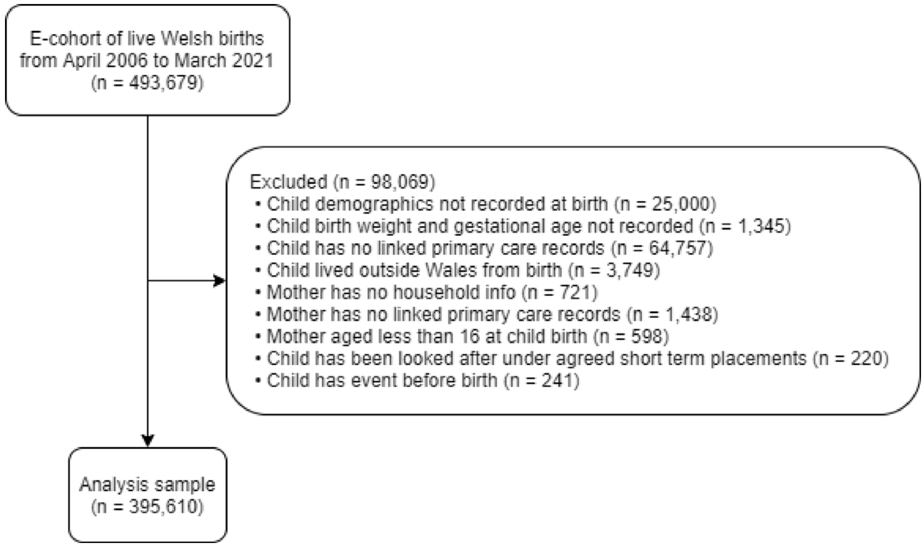

Fig. 2. Sample selection flowchart.

children were excluded from the cohort if they were ever looked after under agreed short-term placements with a local authority. These placements are merely temporary, offering brief respite to parents. Children who had an episode beginning before and spanning birth were included but with the outcome set to occur at birth.

Outcome, exposure and covariates

The main outcome of interest was the risk of becoming a child looked after, measured as the time from birth until the first recorded episode of being looked after. Children who had one episode beginning before and spanning birth were included but with the outcome set to occur at birth. Covariates of interest spanned three categories: maternal demographics, maternal perinatal risk factors and child characteristics (see Table 1).

Maternal demographic covariates consisted of area-level deprivation, the main exposure of interest; cohort period; household composition; and age of mother at child's birth. We allocated each live birth to a quintile of the Welsh Index of Multiple Deprivation (WIMD), a small-area measure of deprivation based on the residing Lower layer Super Output Area. We used five 3-year cohort intervals, assigning each birth to a cohort. Based on the residential anonymised linkage field available in SAIL,[27] we derived the number of children and adults living at the mother's residence in the week of birth.

Maternal perinatal risk factors included mental health problems and several behavioural factors derived from attendances at primary and secondary care services up to 5 years before birth, namely, alcohol problems, substance use, and smoking status. The presence of mental health problems was detected via primary care records only, using clinical codes covering anxiety, depression and treatments for common mental health problems.[28] Alcohol problems covered diagnosis of alcoholism, alcohol-related behaviour or illness in either primary or secondary care records.[29] Substance use was defined either explicitly as "substance use" in primary or secondary care records or as having any problematic behaviour or symptoms related to psychoactive substance use.[29] For mental health, alcohol problems and substance use, we used the date of the latest GP event or hospital admission before birth and categorised it as having occurred either during pregnancy or prepregnancy. We also identified the presence of maternal learning difficulties and disabilities by detecting diagnoses in primary care records for dyslexia or reading, spelling, speech, or arithmetic developmental disorders at any time before child's birth. Smoking status was coded from a self-reported measure at child's birth, which, when missing, was supplemented with primary care records up to 5 years before birth.

Child characteristics included those derived from birth records: sex, ethnic group, congenital anomalies; gestational age; and birth weight. Congenital anomalies were detected through clinical coding of hospital admissions up to 28 days after birth.

Statistical analysis

First, we described the birth cohort in terms of the prevalence of characteristics of interest and the crude event rate at which children became looked after. Second, we used Cox proportional hazard models to analyse the relative risks associated with our measures of interest, with the baseline stratified by the cohort interval in which the mother gave birth, and the main effects included for each covariate. No longer living in Wales and death were treated as competing outcomes, as we censored only if someone does not have either of those or the main outcome by the end of their follow-up. Due to non-proportionality, the number of children living with mother was included with time-varying coefficients; 0–5, 6–11, and $\geq$12 months from the start of the follow-up.

Our models were informed by our a priori directed acyclic graph[30] in Fig. 1. We present three sets of estimates in the tables: unadjusted, adjusted for maternal demographic covariates (WIMD, maternal age, household composition) and fully adjusted for all child and maternal risk factors and demographics. In the narrative description of the results, we highlight the estimates of particular interest, based on Fig. 1, that is, we report demographic-adjusted estimates for the area-level predictor WIMD and mother's demographics and fully adjusted estimates for the risk factors. Finally, we calculated attributable fractions for the main contrasts for each of the covariates at 1-, 5- and 10-year survival time. We did several sensitivity analyses using alternative measures of small-area deprivation and more restrictive sample selection criteria (see Supplementary Material (SM), SM4 Sensitivity analyses). Data preparation and analyses were performed in SQL and R v4.1.

Results

Cumulative incidence of becoming looked after

We identified a cohort of 395,610 children born between 1 April 2006 and 31 March 2021, who were followed up from birth to when

Table 1
Birth cohort's (April 2006 - March 2021) characteristics and event rates of becoming looked after per 1000 person-years.

Characteristic	*n* (%)	Events (rate)
Total	395,610 (100.0%)	7971 (2.7)
Maternal demographics		
Welsh Index of Multiple Deprivation		
1 – Most deprived	108,213 (27.4%)	3702 (4.7)
2	86,722 (21.9%)	1913 (3.0)
3	75,878 (19.2%)	1179 (2.1)
4	61,514 (15.5%)	698 (1.6)
5 – Least deprived	63,283 (16.0%)	479 (1.0)
Age		
16–17	5926 (1.5%)	386 (7.9)
18–19	18,480 (4.7%)	916 (6.1)
20–24	84,337 (21.3%)	2576 (4.0)
25–29	115,584 (29.2%)	2060 (2.5)
≥30	171,283 (43.3%)	2033 (1.6)
Household no. of children		
0 children	149,561 (37.8%)	2770 (2.5)
≥1 children	246,049 (62.2%)	5201 (2.9)
Household no. of adults		
1 adult	89,477 (22.6%)	2268 (3.5)
2 adults	182,459 (46.1%)	3019 (2.2)
≥3 adults	123,674 (31.3%)	2684 (3.0)
Maternal perinatal risk factors		
Learning difficulty/disability		
No	394,452 (99.7%)	7855 (2.7)
Yes	1158 (0.3%)	116 (17.1)
Smoking status		
Non-smoker	240,452 (60.8%)	2592 (1.5)
Ex-smoker	42,849 (10.8%)	678 (2.2)
Smoker	91,995 (23.3%)	4260 (6.1)
Unknown	20,314 (5.1%)	441 (3.1)
Alcohol problems		
Never	393,349 (99.4%)	7650 (2.6)
Prepregnancy	2058 (0.5%)	282 (20.3)
Pregnancy	203 (0.1%)	39 (29.0)
Substance use		
Never	390,540 (98.7%)	7119 (2.5)
Prepregnancy	3906 (1.0%)	585 (22.9)
Pregnancy	1164 (0.3%)	267 (37.2)
Mental health issues		
Never	289,898 (73.3%)	4329 (2.0)
Prepregnancy	87,316 (22.1%)	2822 (4.7)
Pregnancy	18,396 (4.7%)	820 (7.0)
Child characteristics		
Sex		
Male	202,439 (51.2%)	4199 (2.8)
Female	193,171 (48.8%)	3772 (2.7)
Ethnicity		
White	330,429 (83.5%)	7074 (2.8)
Asian	11,989 (3.0%)	135 (1.7)
Black	3757 (0.9%)	59 (2.6)
Mixed	10,236 (2.6%)	229 (3.3)
Other	5435 (1.4%)	72 (1.8)
Unknown	33,764 (8.5%)	402 (3.0)
Congenital anomalies		
No	393,421 (99.4%)	7897 (2.7)
Yes	2189 (0.6%)	74 (4.9)
Preterm birth		
No	367,027 (92.8%)	7105 (2.6)
Yes	28,583 (7.2%)	866 (4.3)
Birth weight		
Low	27,292 (6.9%)	970 (4.9)
Normal	321,798 (81.3%)	6448 (2.7)
Heavy	46,520 (11.8%)	553 (1.6)
Cohort period		
2006/07–2008/09	86,919 (22.0%)	2124 (2.0)
2009/10–2011/12	88,718 (22.4%)	2079 (2.5)
2012/13–2014/15	84,594 (21.4%)	1824 (3.1)
2015/16–2017/18	76,773 (19.4%)	1324 (4.1)
2018/19–2020/21	58,606 (14.8%)	620 (6.6)

they either became looked after, moved out of Wales, died, or reached the end of the study window (Fig. 2).

Table SM6 provides more detail of each step in applying our selection criteria to produce the final analysis dataset. As presented in Table 1, of the 395,610 children in the final data set, 7971 became looked after, at a rate of 2.7 per 1000 person-years. The overall rate of cumulative incidence of becoming CLA from birth is shown in Fig. 3, stratified by birth cohort, deprivation and maternal age. Cumulative incidence curves by each covariate are reported in Supplementary material, Figures SM2-SM5. The rates of CLA increased in more recent birth cohorts and with increasing area deprivation and maternal age.

Perinatal exposures and risk of becoming a child looked after

Fig. 4 shows the hazard ratios (HRs) for the risk of becoming looked after for each of the characteristics that we considered, and Table SM7 in the Supplementary Material reports exact estimates and 95% confidence intervals.

For maternal demographic factors, we found that the greater the area deprivation of the mother's residence, the greater the risk of the child becoming looked after. Children born to mothers living in the most deprived fifth of the population were 3.4 times more likely to enter care compared to those living in the least deprived fifth (demographic adjusted HR [aHR] 3.40, 95% CI 3.08, 3.74). Lower maternal age was strongly associated with the risk of CLA, with maternal age 16–17 years associated with a 3.81 times hazard in the demographic-adjusted estimate, relative to mothers aged ≥30 years (demographic aHR 3.81, 95% CI 3.41, 4.26). With respect to household composition, and relative to households with two adults, mothers living alone had the greatest risk of child removal (demographic aHR 1.28, 95% CI 1.21, 1.135). The presence of other children in the household is associated with lower risk of the relevant child's removal in the first 5 months from birth (demographic aHR 0.58, 95% CI 0.53, 0.62) but increased risk after 12 months (demographic aHR 1.51, 95% CI 1.42, 1.61).

For maternal perinatal risk factors, in the fully adjusted model, maternal mental health problems were associated with an increased risk of their child becoming looked after (fully aHR 2.03, 95% CI 1.88, 2.19). Maternal learning difficulties/disabilities (aHR 3.50, 95% CI 2.91–4.21), current history of smoking (aHR 2.46, 95% CI 2.34–2.60), prior alcohol-related admissions before and during pregnancy (aHR 2, 95% CI 1.76–2.27; aHR 2.35, 95% CI 1.70–3.23, respectively), prior substance use admissions (aHR 3.39, 95% CI 3.09–3.72; aHR 5.72, 95% CI 5.03–6.51 respectively) and history of mental health issues (aHR 1.63, 95% CI 1.55–1.71; aHR 2.03, 95% CI 1.88–2.19, respectively) were all strongly associated with the risk of their child becoming looked after.

With respect to child characteristics, beginning with child-level perinatal risk factors, also in the fully adjusted model, greater risk of care entry was associated with children who were recorded as having congenital anomalies (aHR 1.46, 95% CI 1.16–1.84), of low birth weight (aHR 1.28, 95% CI 1.17–1.39), born preterm (aHR 1.16, 95% CI 1.06–1.26). For child demographic factors, female sex was associated with a lower hazard (aHR 0.93, 95% CI 0.89–0.97) as was unknown ethnicity in the fully adjusted estimates (aHR 0.76, 95% CI 0.68–0.84).

Population attributable fraction

Fig. 5 show the population attributable fraction (PAFs). Considering only potentially modifiable factors and demographic-adjusted estimate, if all children in the two most deprived fifths had the same level of deprivation as those in the least deprived fifth, the risk of CLA would be reduced in the overall population by

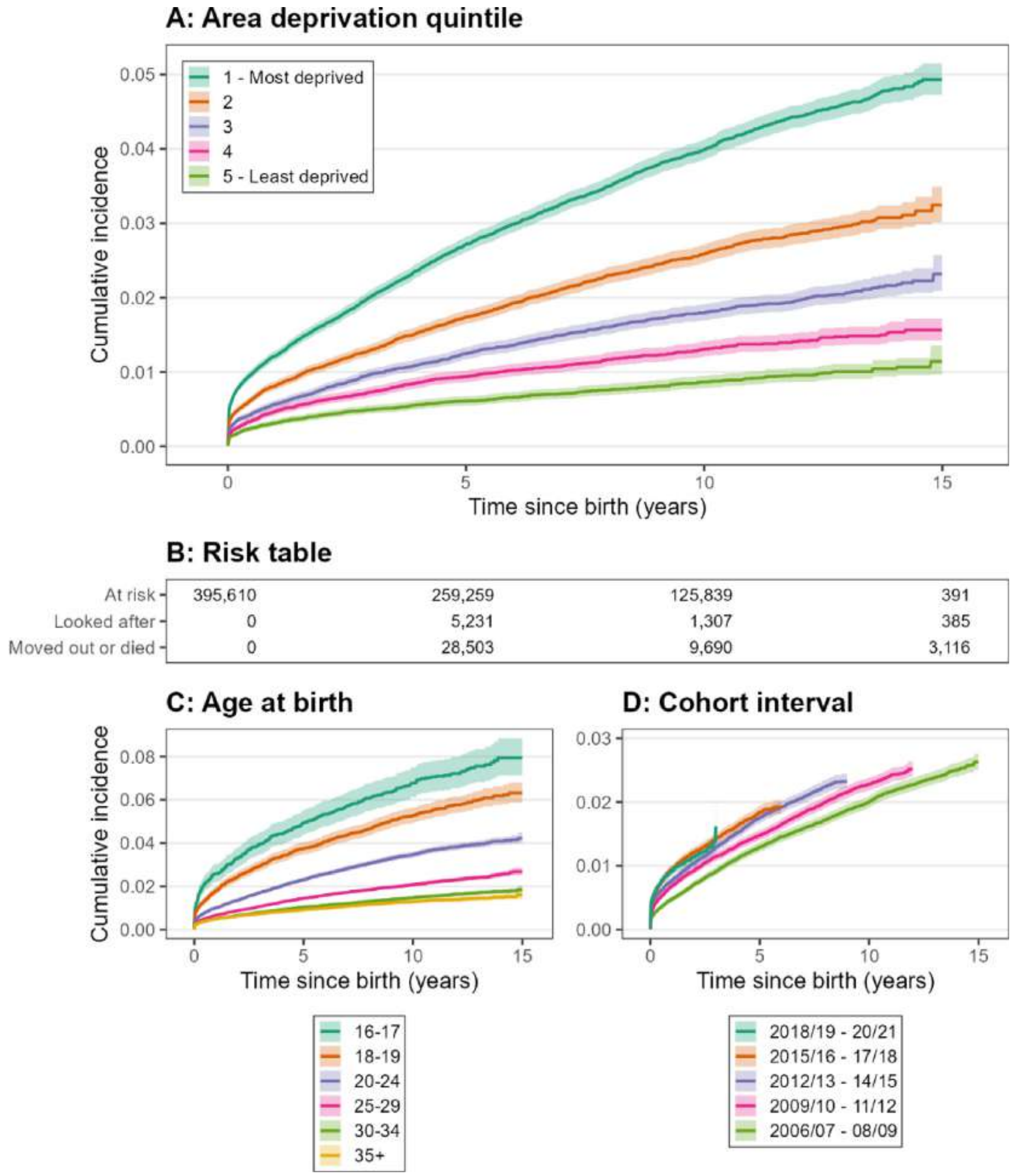

Fig. 3. Overall empirical cumulative incidence of becoming a child looked after, from time since birth, with 95% confidence intervals around the curve. Number at risk and number having had either event is shown below.

around 35% (demographic-adjusted 95% CI 0.33, 0.38). If children in the most deprived fifth had the same level of deprivation as those in the least deprived fifth, the percentage of CLA would be reduced by 22% (demographic-adjusted 95% CI 0.20, 0.24). For the fully adjusted estimates, eliminating maternal mental health issues would potentially reduce the risk of CLA by 20% (fully adjusted 95% CI 0.18, 0.21). Although part of a wider mechanism generating harmful health behaviours, eliminating maternal smoking habits and substance use might reduce the burden of CLA by 27% (fully adjusted 95% CI 0.26–0.29) and 7% (fully adjusted 95% CI 0.07–0.08) respectively.

Robustness checks and additional analyses

Our sensitivity analyses found that Townsend Index in place of WIMD as a measure of area deprivation produced similar results. Our findings did not change when using the more restrictive sample selection criteria, and slight increases were found for the effects of area deprivation when considering only outcomes captured using the routinely generated linkage keys, although the trend across the categories was the same as our main analysis (see Supplementary Material (SM), SM4. Sensitivity analyses).

Discussion

In a whole population sample of around 400,000 children born in Wales, we used linked, routinely collected data to assess demographic, maternal and child-level risk factors for children becoming looked after, measured in the perinatal period. Our findings are consistent with a limited UK literature on individual-level risk factors for becoming looked after which nevertheless highlights the powerful role of adverse socio-economic conditions

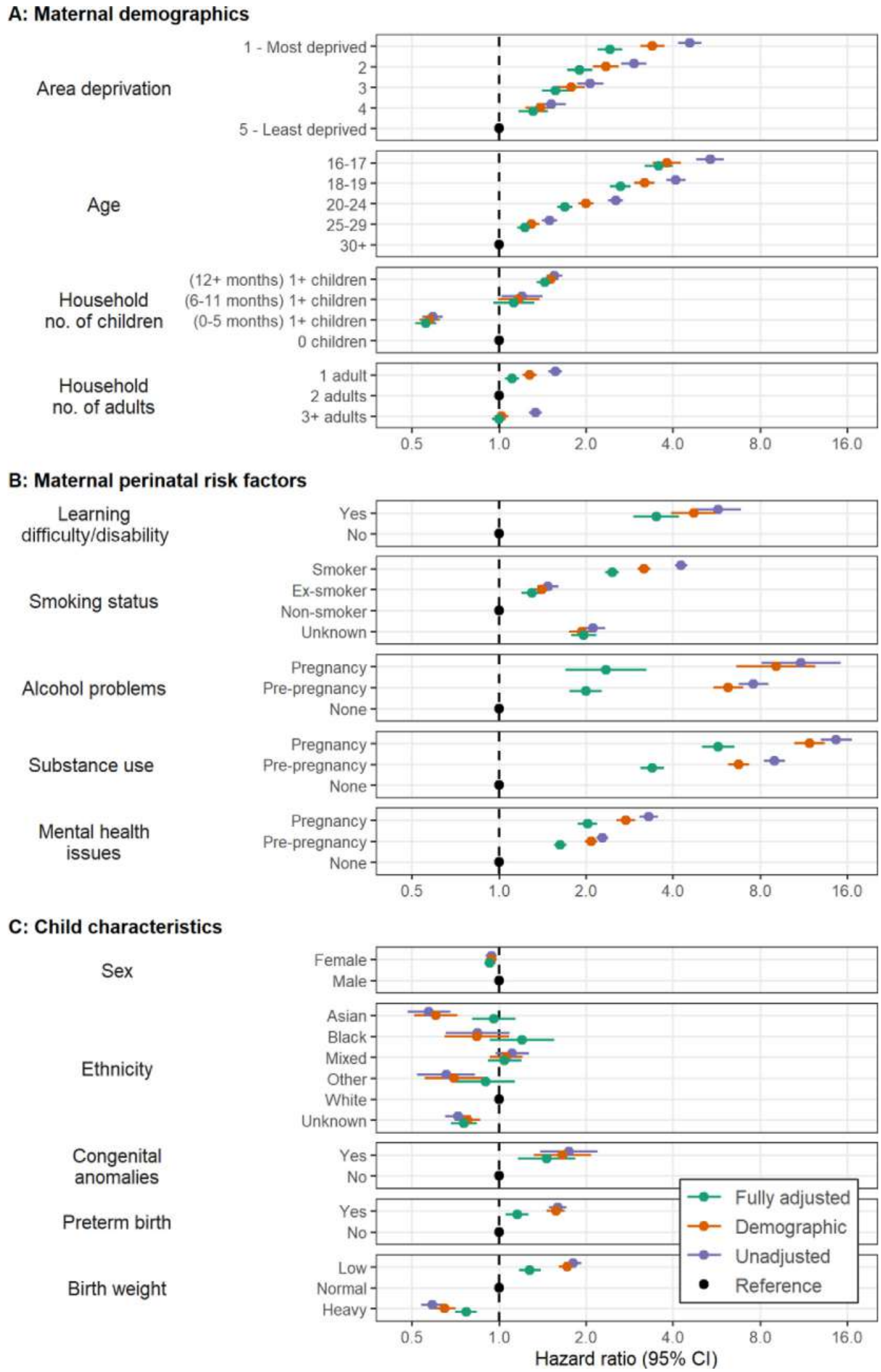

Fig. 4. Unadjusted, demographic-adjusted and fully adjusted hazard ratios for the risk of becoming looked after, with 95% confidence intervals.

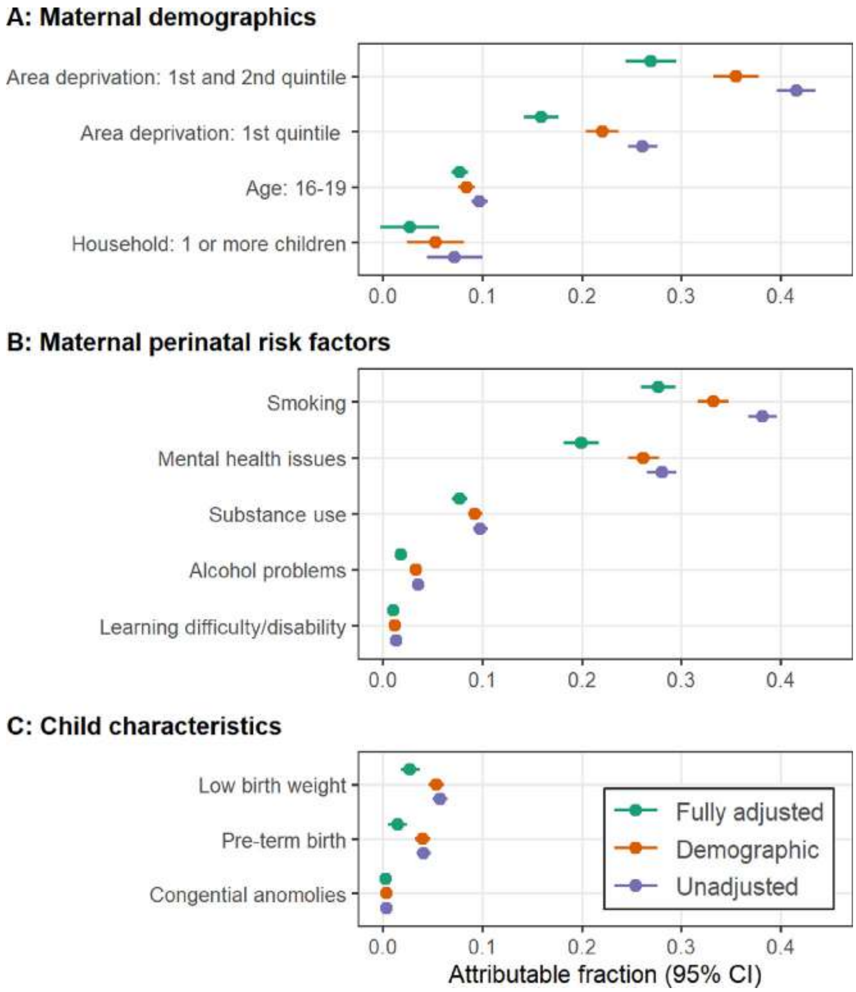

Fig. 5. Unadjusted population attributable fractions for key mother and child indicators after 1, 5 and 10 years of survival time, with 95% confidence intervals.

in the perinatal period in structuring the risk of care entry. We demonstrate stark inequalities in rates of children entering care and strong associations with a range of maternal demographic and perinatal factors and child characteristics. Mothers living in the most deprived fifth of WIMD were almost three and a half times more likely to have their children taken into care than those living in the least deprived fifth of the population. Mothers of children taken into care were more likely to be younger, to live in a household with no other adults, or more than two adults, and to live with other children during the new-born's first year of life; they were also more likely to experience mental health problems and learning difficulties and disabilities and were more likely to have alcohol problems, smoke and use substances. Children taken into care were more likely to be born male, preterm, with low birth weight, and have recorded congenital anomalies.

Regarding our estimates of the burden of CLA attributable to modifiable exposures, they align with the literature pointing to a contributory direct causal effect on care entry of adverse socio-economic conditions.[14–16,24,31] An evidence review[31] outlines two theoretical models for the relationship between poverty and child maltreatment – the family stress model, whereby poverty clusters with the adversities it produces, contributing to poor outcomes; and the investment model, whereby families lack the material and social to invest in children, leading to increased risk of neglect and care entry. These conditions contribute to poor child health and well-being also via their adverse impact on maternal mental health, itself an important risk factor for care entry.[15,16,18,19,24] Policies that directly address the socio-economic conditions in which expectant mothers live, and into which children are born, are likely to have a meaningful impact on the population-level risk of CLA. If children in the most deprived areas of Wales were to experience the same conditions as those in the least deprived, the population-level risk of CLA could be reduced by more than a third.

Based on our results, in an alternative policy scenario, successfully tackling maternal mental health issues might reduce the risk of CLA, and within an ideal scenario, our study estimates that eliminating maternal mental health problems would reduce the risk by as much as 20%. Poor maternal mental health as assessed during, or in the several years before pregnancy, was consistently associated with higher risk of children entering care in the literature.[16,19] Our finding that parents with learning difficulties and disabilities were more likely to have a child taken into care aligns with a study exploring the overrepresentation of parents with intellectual and development disabilities in the US child protection system.[18]

Of other perinatal maternal risk factors identified in our study, smoking before birth and substance use also appeared in the literature, as did alcohol use.[16,23] Reflecting socio-economic disadvantage and health behaviour associated with allostatic load, where allostatic load is defined as the cumulative burden of chronic stress and adverse life events,[32] the large PAF for maternal smoking may be attributable to a range of unmeasured social support and mental health–related factors associated with both smoking habits and care entry.[16] The same may be true of the smaller PAF for substance use and alcohol abuse in pregnancy.[13,15,23] Policies that support women to tackle addiction or harmful health behaviours, family planning strategies targeting young people, and additional support for young expectant mothers, may have positive impacts on the risk of care entry.

With respect to child-level characteristics, our results parallel those from other studies identifying an increased risk of care entry for children with birth anomalies, born preterm, and of low birthweight.[6,21] Unsurprisingly, due to the ethnic composition of the Welsh population (around 95% White), and the ascertainment of the measure used in this study, our results do not shed further light on ethnicity and CLA.

Socio-economic conditions appear to offer a consistent frame within which to understand the role of other major risk factors. Further research should aim to use causal mediation methods to understand causal pathways in deprivation, adversity and risk of being looked after to disentangle processes and identify policy entry points.

Strengths and limitations

The key strength of this study is its use of one of the UK's largest linked administrative data sets, newly encompassing longer-term children's social care data, to identify individual-level risk factors for becoming looked after, with longitudinal data linkage over a 15-year period. Using this data set, we developed improved methods for identifying children who became looked after, so reducing bias. These data also allow for improved temporal modelling of exposures and outcomes while controlling for death and emigration as competing risks, improving the certainty of our findings.

Our application of restrictions to the denominator population, based on the availability of complete data on linkage fields and relevant indicators, constitutes a limitation. We also excluded from our analysis individuals from primary care practices that do not share their data with SAIL. Moreover, and despite improved linkage, complete ascertainment of the outcome was not possible, and we were unable to observe the entire CLA population between 2006 and 2021. As a result, we expect our estimates to be conservative and to potentially understate the impact of deprivation and other factors on the risk of CLA.

With respect to the covariates considered in this analysis, we were unable to measure other potential indicators of risk, such as involvement with the criminal justice system. Nor did we take into account child developmental and learning difficulties and disabilities, as these are only reliably measured postnatally. Children's learning difficulties and disabilities are a major risk factor for care entry in developed countries[14] and should be considered in future studies. Finally, the validity of PAFs rests on the assumption that the relationship between exposure and outcome approximates a true causal effect. They should therefore be interpreted with caution.

Implications for policy and practice

Rising deprivation and poverty appear to be major drivers of care entry. Given the wider context of ongoing austerity, rising poverty and cuts to preventative services for children in the United Kingdom, our findings are concerning. The vicious cycle of rising poverty, ever-increasing social spending on children who have been removed from their family and cuts to prevention services is magnified and perpetuated by the long-term poor health, social and educational outcomes of the increasing care experienced by population.[10] In both Wales and England, cuts to preventative children's services have occurred at the same time as rising spend on CLA.[7,8] Our analysis supports the view that approaches such as raising thresholds for care are unlikely to be effective without sustained attention to the wider determinants of child health.

We argue for the need to consider the compound effect of poverty and maternal health conditions on the risk of CLA, as a social policy and public health priority. At national level, increasing household income for families with children through the welfare benefits system is likely to be an effective strategy. Increasing funding to local authorities responsible for delivering preventative services proportional to need[11] may help strengthen the fragile child protection system. At local level, services offering benefits and debt advice, free childcare and respite may help mitigate the impact of disadvantaged socio-economic conditions on care entry. Within social services, effective interventions should occur as early as possible in pregnancy, particularly among disadvantaged mothers. These might include preventive maternal support services, including financial, mental health and community support. This should take precedence over child removal whenever possible.

Preventing CLA status through family-support measures, we believe, could play a prominent role in reducing the growing expenditure on escalating life course disadvantage, counteracting the lower educational outcomes, higher mortality rates and higher rates of hospital admissions and criminal justice system involvement experienced by the CLA population.

Author statements

Ethical approval

Ethical approval was sought and obtained by the authors to access pseudonymised and deidentified data from administrative sources and health records through the ethical approval committee of the SAIL Databank.

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Competing interests

The authors declare no competing interests.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.puhe.2023.09.001.

References

1. Bennett DL, Mason KE, Schlüter DK, Wickham S, Lai ETC, Alexiou A, et al. Trends in inequalities in Children Looked after in England between 2004 and 2019: a local area ecological analysis. *BMJ Open* 2020;**10**:e041774.
2. Hodges H. *Children looked after in Wales: trends*. 2020.
3. Thomas C. *The Care Crisis Review: factors contributing to national increases in numbers of looked after children and applications for care orders*. 2018.
4. Bennett DL, Schlüter DK, Melis G, Bywaters P, Alexiou A, Barr B, et al. Child poverty and children entering care in England, 2015–20: a longitudinal ecological study at the local area level. *Lancet Public Health* 2022;**7**:e496–503.
5. Hodges H, Bristow D. *Analysis of the factors contributing to the high rates of care in Wales briefing paper*. 2019.
6. Griffiths LJ, Johnson RD, Broadhurst K, Bedston S, Cusworth L, Alrouh B, et al. Maternal health, pregnancy and birth outcomes for women involved in care proceedings in Wales: a linked data study. *BMC Pregnancy Childbirth* 2020;**20**: 1–13. 2020 201.
7. The County Councils Network. *The association of county chief executives & Newton europe*. The future of children's social care; 2022.

8. ADSS Cymru & CLILC WLGA. *WLGA and ADSS cymru position statement on children's services*. 2018.
9. Sebba J, Berridge D, Luke N, Fletcher J, Bell K, Strand S, et al. *The educational progress of looked after children in England: linking care and educational data*. 2015.
10. Xie T, de Mestral C, Batty GD. Association of public care in childhood with social, criminal, cognitive, and health outcomes in middle-age: five decades of follow-up of members of the 1958 birth cohort study. *J Epidemiol Community Health* 2021;**75**:289–96.
11. Webb CJR. More money, more problems? Addressing the funding conditions required for rights-based child welfare services in England. *Societies* 2022;**12**.
12. Bilson A, Bywaters P. Born into care: evidence of a failed state. *Child Youth Serv Rev* 2020;**116**.
13. O'Donnell M, Maclean MJ, Sims S, Morgan VA, Leonard H, Stanley FJ. Maternal mental health and risk of child protection involvement: mental health diagnoses associated with increased risk. *J Epidemiol Community Health* 2015;**69**:1175–83.
14. Simkiss DE, Stallard N, Thorogood M. A systematic literature review of the risk factors associated with children entering public care. *Child Care Health Dev* 2013;**39**:628–42.
15. O'Donnell M, Maclean M, Sims S, Brownell M, Ekuma O, Gilbert R. Entering out-of-home care during childhood: cumulative incidence study in Canada and Australia. *Child Abuse Negl* 2016;**59**:78–87.
16. Green MJ, Kariuki M, Chilvers M, Butler M, Katz I, Burke S, et al. Inter-agency indicators of out-of-home-care placement by age 13–14 years: a population record linkage study. *Child Abuse Negl* 2019;**93**:91–102.
17. Canfield M, Radcliffe P, Marlow S, Boreham M, Gilchrist G. Maternal substance use and child protection: a rapid evidence assessment of factors associated with loss of child care. *Child Abuse Negl* 2017;**70**:11–27.
18. LaLiberte T, Piescher K, Mickelson N, Lee MH. Child protection services and parents with intellectual and developmental disabilities. *J Appl Res Intellect Disabil* 2017;**30**:521–32.
19. Ranning A, Munk Laursen T, Thorup A, Hjorthoj C, Nordentoft M. Serious mental illness and disrupted caregiving for children: a nationwide, register-based cohort study. *J Clin Psychiatry* 2015;**76**:e1006–14.
20. Högberg U, Sennerstam R, Wester K, Högberg G, Andersson J, Thiblin I. Medical diagnoses among infants at entry in out-of-home care: a Swedish population-register study. *Heal. Sci. Reports* 2019;**2**:e133.
21. Needell B, Barth RP. Infants entering foster care compared to other infants using birth status indicators. *Child Abuse Negl* 1998;**22**:1179–87.
22. Ahmed N, James D, Tayabali A, Watson M. *Ethnicity and children social care*. 2022.
23. Hafekost K, Lawrence D, O'Leary C, Bower C, O'Donnell M, Semmens J, et al. Maternal alcohol use disorder and subsequent child protection contact: a record-linkage population cohort study. *Child Abuse Negl* 2017;**72**:206–14.
24. Wall-Wieler E, Roos LL, Brownell M, Nickel NC, Chateau D. Predictors of having a first child taken into care at birth: a population-based retrospective cohort study. *Child Abuse Negl* 2018;**76**:1–9.
25. Lyons RA, Jones KH, John G, Brooks CJ, Verplancke J-P, Ford DV, et al. The SAIL databank: linking multiple health and social care datasets. *BMC Med Inf Decis Making* 2009;**9**.
26. Allnatt G, Lee A, Scourfield J, Elliott M, Broadhurst K, Griffiths L. Data resource profile: children looked after administrative records in Wales. *Int. J. Popul. Data Sci.* 2022;**7**.
27. Johnson RD, Griffiths L, Hollinghurst JP, Akbari A, Lee A, Thompson DA, et al. Deriving household composition using population-scale electronic health record data-A reproducible methodology. *PLoS One* 2021;**16**.
28. John A, McGregor J, Fone D, Dunstan F, Cornish R, Lyons RA, et al. Case-finding for common mental disorders of anxiety and depression in primary care: an external validation of routinely collected data. *BMC Med Inf Decis Making* 2016;**16**(1):1–10. 2016 16.
29. Kuan V, Denaxas S, Gonzalez-Izquierdo A, Direk K, Bhatti O, Husain S, et al. A chronological map of 308 physical and mental health conditions from 4 million individuals in the English National Health Service. *Lancet Digit. Heal.* 2019;**1**:e63–77.
30. Pearl J. *Causality: models, reasoning, and inference*. 2nd ed. Cambridge University Press; 2010.
31. Bywaters P, Bunting L, Davidson G, Hanratty J, Mason W, McCartan C, et al. *The relationship between poverty, child abuse and neglect: an evidence review*. 2016.
32. Mcewen BS. Allostasis and allostatic load: implications for neuropsychopharmacology. *Neuropsychopharmacology* 2000;**22**.

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Review Paper

Integrating social determinants of health in medical education: a bibliometric analysis study

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ABSTRACT

Objectives: Social determinants of health (SDH) are the prevalent enablers of health among populations, and integrating them in medical education will advance clinical care by integrating social and economic risk data into medical diagnosis and treatment. Despite the numerous publications on SDH and medical education, the publication trends are not known. The study aims to analyse publication trends in integrating SDH into medical education and the corresponding thematic areas.
Study design: This was a bibliometric analysis study.
Methods: Bibliometric was used. Data from Scopus databases from January 2006 to June 2023 were retrieved with no language restriction. VOSviewer software was used for analysis. Bibliographic coupling was used to identify the clusters of published literature on the integration of SDH into medical education, followed by the analysis of annual distribution and growth trends, authors and co-author relationships and collaborations.
Results: A total of 1047 articles were retrieved. The annual research publication exhibited a swift surge in the studies conducted during the reviewed period. Five clusters of information were derived: relating to curriculum development, community engagement and service-learning, stakeholder collaborations, development of assessment methods and tools for SDH, and the impact of integrating SDH into medical education.
Conclusion: Bibliometric analysis has revealed a growing trend in the field of integrating SDH into medical education, and the study has highlighted the research impact through bibliographic coupling by identifying the five thematic areas. This study lays a foundation for advancing knowledge on what has been published and possible areas for improvement in the integration of SDH into medical education.

Introduction

The World Health Organisation defines social determinants of health (SDH) as peoples' non-medical conditions that influence health outcomes and quality of life, such as where they are born, grow, live, work and age.[1] Recent studies have noticed the significant contribution of social, economic and behavioural factors in promoting or altering population health outcomes.[2–4]

Socio-economic factors have demonstrated significant contributions to disparities in health and well-being among populations. For instance, within the socio-economic scale, those at the top are likely to have better health outcomes compared with the middle class. Similarly, those at the lower scale are likely to experience worse health outcomes compared with those at the middle.[5]

Integration of the SDH in medical education and the healthcare system will advance clinical care by integrating social and economic risk data into medical diagnosis and treatment. With socio-economic factors being barriers to the delivery of high-quality care, this integration will guide community partnerships and clinical encounters in improving health outcomes.[6]

Studies have demonstrated that apart from gaining broad perspectives on health disparities, medical students will obtain satisfaction and self-efficacy when engaging with the communities they serve.[7] Not only does this amplify their engagements but also enhances their skills in addressing emergent health needs within the communities. However, for medical education to address the SDH, a multidimensional and multifaceted approach that incorporates

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traditional didactic teachings, community-based learning opportunities and decisively conventional role modelling is needed. In addition, the curricula content should also integrate experiential learning and an enhanced SDH-oriented clinical learning environment.[8]

Previous studies spanning from 2006 have focused on various models, strategies and frameworks applied in teaching, assessment and evaluation of the medical curriculum.[9] Over that period, substantial progress and trends in SDH incorporation into medical education can be noticed. For a clear demonstration of this progress, a bibliometric analysis was deemed the most suitable method for the present study.

Bibliometrics analysis was initially introduced in 1989 by Alan Pritchard,[10] and since then, it has received broader attention particularly due to the advancements in evidence science, access to computers, availability of the internet and availability of bibliometrics software, such as VOSviewer, CiteSpace and Biblioshiny.[11,12] Outstanding advancements have also been made in the development of scientific databases that work with bibliometric software packages, such as the Web of Science, Scopus and PubMed.[13]

In bibliometric analysis, statistics from available databases are used to demonstrate the distribution of contributions, hotspots and projected trends of a particular field. As a vital tool for analysis, bibliometrics helps to investigate researchers' findings and how they integrate or make sense in the broader academic and intellectual fields.[12]

VOSviewer is among the bibliometric software used for data analysis and visualisation.[14] This software can posit knowledge domains by generating and visualising co-occurrence network maps of co-authors, keywords and co-citation networks of cited authors based on the bibliographical archives gathered from a particular database.[15]

Although studies on integrating SDH into medical education have gained worldwide attention, there are no published bibliometric studies related to this topic. To bridge this gap, we used Scopus databases to perform a bibliometric study of the documents published in the field of integrating SDH into medical education. The study applied VOSviewer for data analysis and visualisation. Bibliographic coupling was used to cluster the documents into various thematic areas.

Methods

Study design

Bibliometric was applied in analysing trends of the published literature on integrating SDH into medical education.[14] VOSviewer was used for data analysis and visualisation[16,17] The bibliometric analysis was carried out using documents retrieved from the Scopus database (https://www.scopus.com/). Scopus database has wider coverage with over 25,100 journals and access to 1.7 billion citations.[18,19–21] Scopus data (January 2006 to June 2023) were abstracted on 4 May 2023. All retrievals were done in 1 day to steer clear of variations due to daily updates, and the following search strategy was applied: "social determinants of health" OR SDH OR sdh AND teaching OR "medical education" OR "medical curriculum" OR "educational model" OR "medical school." The search excluded studies that were undertaken before January 2006, and we limited our search to publications that were only carried in the English language. Manual search from the references of the retrieved documents was done to ensure that all relevant references were included in the study.

Data analysis

Co-authorship analysis, co-occurrence analysis, citation analysis, bibliographic coupling and co-citation analysis of the Scopus data were done using VOSviewer software. Bibliographic coupling, which is the measure of an object's connectedness based on the number of references they share, was used to highlight the parallels between the two works' subjects in terms of documents, sources, authors and organisations.

Results

Yearly distribution and growth trend

A total of 1047 documents were retrieved. The first article on SDH in medical education was published in 2006,[4] and since then, there is a steady increase in the number of publications, which is a probable demonstration of the significance of the research topic (Fig. 1).

Distribution of publications on a country-by-country basis and total link strength

Articles from 40 countries were retrieved, with the United States having the highest volume of published manuscripts ($n = 644$), followed by the United Kingdom ($n = 95$) and Canada ($n = 90$). Cumulatively, at least 15 countries published at least 10 articles in the research field, and in terms of the total percent of published articles, the United States, the United Kingdom, Canada, Australia and India had a cumulative percentage of 78% of all the articles published. In terms of the number of citations per country during the period under review, the United States was leading ($n = 8249$), followed by Canada ($n = 2949$) and Sweden ($n = 2137$). Regarding the average citation per document, Sweden was leading with an average of 164.38 citations per document. The United States ranked first in terms of total link strength ($n = 221$), followed by Canada ($n = 134$) and the United Kingdom ($n = 78$).

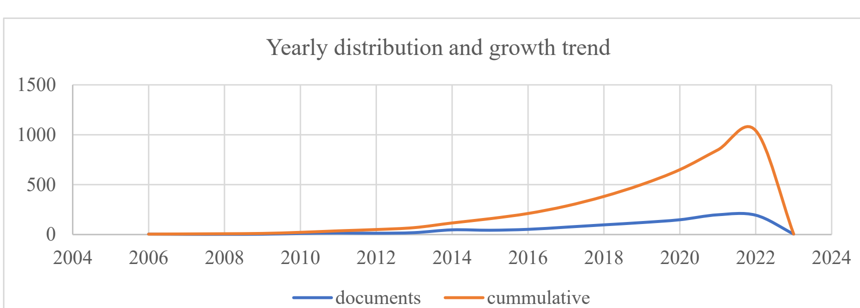

Fig. 1. Annual changes in the number of publications and the total number of publications.

Table 1
Leading organisations/institutions with over three publications.

S/No	Organisation	Country	Documents	Citations	Average citation per document	Total link strength
1	Harvard Medical School, Boston	USA	9	75	8.3	1
2	Yale School of Medicine, New Haven	USA	7	142	20.3	2
3	Penn State College of Medicine, Hershey	USA	4	107	26.6	1
4	Boston University School of Medicine	USA	3	10	3.3	0
5	The University of Nebraska Medical Centre	USA	3	9	3	2
6	University of Toronto, Toronto	Canada	3	36	12	0
7	Oregon Health and Science University	USA	3	29	9.7	0
8	University of Ottawa, Ottawa	Canada	3	61	20.3	0
9	Icahn School of Medicine at Mount Sinai	USA	3	3	1	1
10	University College London, London	UK	6	39	6.5	0

The organisation with the most publications were the Harvard Medical School ($n = 9$), the Yale School of Medicine ($n = 7$) and University College London ($n = 6$). Regarding the total number of citations, Yale School of Medicine was leading ($n = 142$), followed by Penn State College of Medicine ($n = 107$; Table 1).

Authors and co-author relationships

The cumulative number of articles published and the citation metrics achieved by the authors were used to classify the most engaged researchers in the field of SDH and medical education. Klein had the highest number of documents ($n = 10$), followed by Serwint ($n = 8$) and Gonzalo ($n = 6$). The following authors had the highest citations: Klein ($n = 201$), Simon ($n = 189$), Gonzalo ($n = 137$) and Kaufman ($n = 109$).

Journals publishing articles relating to SDH and medical education

The journal that had the largest number of documents on the research topic was Academic Medicine Journal. A total of 53 articles were published in the period under review, with a sum of 1181 citations. The second journal was the BMC Medical Education Journal, with 29 articles and 254 citations, and the third was MedEd Portal: The Journal of Teaching & Learning Resources, with 24 documents and 146 citations. The average number of citations per document suggests the significance of articles published in the journal. In the present study, the Lancet had the highest average total citations per document (documents: 11, average citation per document: 197.2), followed by the New England Journal of Medicine (documents: 13, average citation per document 44.8) and the Academic Medicine Journal (documents: 53, average citation per document: 22.3; Table 2).

Documents, citation relationships and collaboration network between countries

The association between the published articles and citations attained is a significant marker of the quality of the published articles. Improved citation count is a characteristic of the outstanding quality of the published document, resulting in a better number of citations by other researchers in the same field. In the present study, documents that had been cited more than 30 times were selected. Publications that had the highest citations were authored by Bozorgmehr, 2011 ($n = 121$), Klein, 2011 ($n = 91$), Colvin, 2016 ($n = 90$) and Mangold, 2019 ($n = 79$). Regarding the collaboration network between institutions and organisations, Harvard School of Medicine had the highest network of research collaborators, whereas the other institutions collaborated on a small scale (Table 3).

The analysis of bibliographic coupling

The potential association between SDH and medical education was assessed using bibliometric coupling. Through VOSviewer, 51 articles were selected from the original data according to their coupling strength (the selected articles received at least 40 citations each). As demonstrated in Fig. 2, a total of five clusters were identified and presented with different node colours. The articles aligned to each coloured node were analysed independently to align them to correct thematic areas related to the integration of SDH into medical education. The first cluster

Table 3
Top cited articles in the research topic.

S/No	Document	Citations	Links	References
1	Bozorgmehr K. (2011)	121	0	22
2	Klein M.D. (2011)	91	2	23
3	Colvin J.D. (2016a)	90	1	24
4	Mangold K.A. (2019)	79	0	25
5	Dharamsi S. (2010)	62	0	26
6	Kasper J. (2016)	61	1	27
7	Klein M.D. (2014)	58	2	28
8	Sartorius B.K.D. (2014)	44	0	29
9	Gonzalo J.D. (2017)	41	0	30
10	Knight S.E. (2016)	37	0	31

Table 2
Top 10 journals published most articles on the research topic.

S/No	Source	Documents	Citations	Average citation per document	Total link strength
1	Academic Medicine	53	1181	22.3	85
2	BMC Medical Education	29	254	8.8	46
3	MedEd Portal: The Journal of Teaching & Learning Resources	24	146	6.1	6
4	Journal of General Internal Medicine	22	245	11.1	32
5	Medical Teacher	19	283	14.9	33
6	International Journal of Environmental Research & Public Health	18	69	3.8	1
7	Academic Paediatrics	17	270	15.9	23
8	New England Journal of Medicine	13	582	44.8	10
9	Education for Primary Care	11	39	3.5	11
10	The Lancet	11	2169	197.2	1

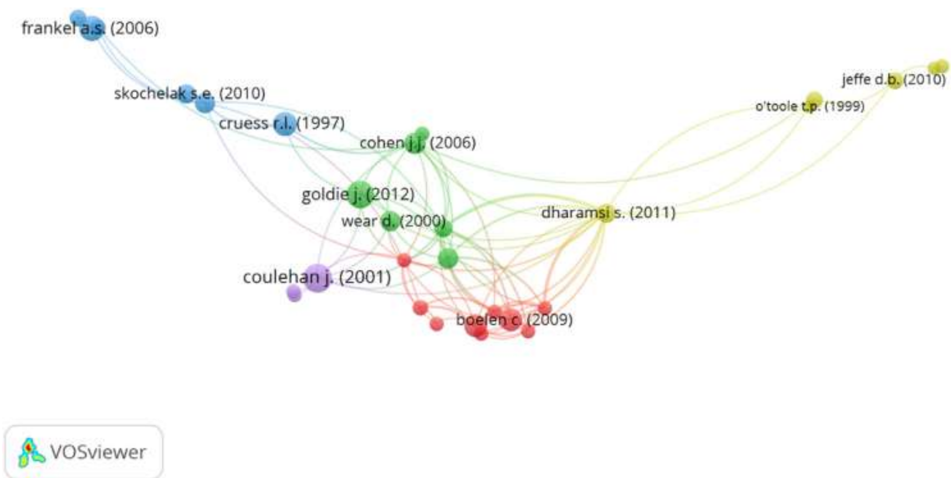

Fig. 2. Bibliographic coupling.

(yellow nodes) focuses on curriculum development so that medical schools can teach topics, such as health disparities, health equity, and the impact of social factors on health, such as education, housing and discrimination. The second cluster (green nodes) focuses on community engagement and service-learning. In this thematic area, the emphasis is to inspire medical students to engage with underserved communities and participate in service-learning experiences. The third cluster (red nodes) focuses on partnerships and stakeholder collaboration with key players in the health sector to increase the understanding of the need for integrating SDH into medical education. The collaboration will provide valuable insights into community health initiatives and policies that are addressing the integration of SDH into medical education. The fourth cluster (purple nodes) focuses on the development of assessment methods and tools that are used to measure the attitudes of students, faculty, stakeholders and the community towards the incorporation and implementation of the concept of integrating SDH into medical education. The last cluster of articles (blue nodes) focuses on the impact of integrating SDH into medical education. The reviewed articles indicated several positive impacts, including improved patient care through community engagements, reduced health disparities and improved collaboration between the medical school and other stakeholders (Fig. 2).

Discussion

Bibliometric analysis of the studies on the integration of SDH into medical education was conducted by use of VOSviewer software, and the authors preferred Scopus database, as it has more benefits compared with other scientific databases.[13]

Most published literature were from the United States, and the top organisations publishing more than three articles were from the United States, Canada, and the United Kingdom. Given the extensive influence of SDH, developed countries have embarked on teaching modules that inform trainee physicians about SDH and how they impact health. As demonstrated by numerous studies, partnerships and collaborations between academic medical centres and community-based organisations have the potential to create a feasible, effective and sustainable platform to prepare medical students for SDH.[32] The studies have also established the role of educational technologies and pedagogies in facilitating internationally interconnected styles in the medical curriculum, which emphasise the mobility of learners and educators across borders.[33]

The growing number of published literature and the citation metrics drawn by the authors were categorised based on the most involved researchers in the field. Klein had the highest number of publications, and in all his work, he has demonstrated the need to train physicians on SDH and develop their skills to assess for social and environmental risks within divergent populations. Klein also noted that the educational intervention would enhance applicable knowledge among physicians and improve the traditional medical curricula, which do not specifically address families' social, economic and environmental needs.[23]

A comprehensive analysis of the institutions working on the integration of SDH into medical education was given. This finding is significant, particularly to upcoming researchers, as this would guide them by presenting a strong background knowledge of the study topics that have been covered in the research field and practicable research gaps. This knowledge also presents a base for networking with peers who have significant proficiency in the field of study, while interdisciplinary work may provide an effective approach to address the identified research gaps.[34]

Another substantial finding in this study includes the five thematic areas identified through bibliographic coupling. The five thematic areas include curriculum development, community engagement and service-learning, stakeholder collaborations, the development of assessment methods and tools for SDH, and the impact of integrating SDH into medical education. This finding is in line with the existing SDH frameworks, which demonstrate similar strategies of SDH integration, such as community partnerships, service-learning and curriculum development.[35]

The main study limitation was the dependence on the Scopus database, which is subject to continuous change and updating in the number of indexed articles. Similar to all other scientific databases, there is a likelihood of discrepancies in the results after a short period, as more researchers are exploring the research topic. The VOSviewer tool would only undertake comprehensive analysis using Scopus data set. VOSviewer is unable to provide other types of visualisation beyond network graphs. Therefore, the developers of VOSviewer should consider reviewing the software to accommodate all functions when analysing other scientific databases just like the Scopus data set. These may include simple line charts showing the growth of paper by keywords to more complex network trend topic analysis visualisations to temporal trend analysis. The software can be improved to offer a thematic analysis option that plots clusters of keywords along two dimensions (density vs centrality).

This will be crucial in spotting emerging clusters and the degree of importance of each cluster.

Conclusion

This was the first bibliometric study on SDH and medical education. There is a steady increase in the number of published articles since 2006. The publications are mainly in five thematic areas, focusing on curriculum development, community engagement and service-learning, stakeholder collaborations, development of assessment methods and tools for SDH and the impact of integrating SDH into medical education. This study lays a foundation for advancing knowledge on what has been published and possible areas of improvement in the integration of SDH into medical education, such as investing in stakeholder collaborations, experiential learning and community participation in the identification of the priority health needs that the medical schools can attempt to resolve.

Future research direction

The study's findings indicate the importance of exploring ways to integrate the SDH curriculum into broader educational programs, making it universally accessible. It is also imperative to consider how to seamlessly incorporate the SDH curriculum into clinical education across all training sites. This approach will significantly enhance the educational impact by providing trainees with essential integrative skills that validate the training program's value.

Finally, there is a need to research on specific competencies needed in the identification and mitigation of SDH. This may include the recognition of implicit and explicit biases, advocacy skills, development of a basic awareness of healthcare financing and payment structures and communication skills needed to unravel the socio-economic barriers to effective clinical care.

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Ethical approval

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Competing interests

None declared.

References

1. WHO. Social determinants of health [internet]. *World Health Organisation* 2022 [cited 2022 Nov 11], Available from: https://www.who.int/health-topics/social-determinants-of-health#tab=tab_1.
2. Friedman NL, Banegas MP. Toward addressing social determinants of health: a health care system strategy. *Perm J [Internet]* 2018;**22**(4S) [cited 2023 Jan 14].
3. Braveman P, Gottlieb L. *The social determinants of health: it's time to consider the causes of the causes*. 2014. 101177/00333549141291S206 [Internet]. [cited 2023 Jan 14];129(SUPPL. 2):19–31, Available from: https://journals.sagepub.com/doi/abs/10.1177/00333549141291S206.
4. Irwin A, Valentine N, Brown C, Loewenson R, Solar O, Brown H, et al. The commission on social determinants of health: tackling the social roots of health inequities. *PLoS Med [internet]* 2006 [cited 2023 Jan 13];3(6):e106, Available from: https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.0030106.
5. Stringhini S, Sabia S, Shipley M, Brunner E, Nabi H, Kivimaki M, et al. Association of socioeconomic position with health behaviors and mortality. *JAMA [Internet]* 2010;**303**(12):1159–66 [cited 2023 Jan 14], Available from: https://jamanetwork.com/journals/jama/fullarticle/185584.
6. Gottlieb L, Fichtenberg C, Alderwick H, Adler N. Social determinants of health: what's a healthcare system to do? *J Healthc Manag* 2019;**64**(4):243–57.
7. Martinez IL, Artze-Vega I, Wells AL, Mora JC, Gillis M. Twelve tips for teaching social determinants of health in medicine. *Med Teach* 2015;**37**(7):647–52.
8. Siegel J, Coleman DL, James T. Integrating social determinants of health into graduate medical education: a call for action. *Acad Med* 2018;**93**(2):159–62.
9. Gard LA, Bartell T, Shah AK, Setrini AB, Sheehan K, Miller CH, et al. Interprofessional education in medical-legal partnerships (MLPs) to address social determinants of health. *J Health Care Poor Underserved [Internet]* 2021;**32**(4):1720–33. Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med20&NEWS=N&AN=34803038.
10. Statistical AP. Bibliography or bibliometrics. *J Doc [Internet]* 1969;**25**:348 [cited 2022 Dec 6], Available from: https://cir.nii.ac.jp/crid/1570009750342049664.
11. Aria M, Cuccurullo C. bibliometrix: an R-tool for comprehensive science mapping analysis. *J Informetr* 2017;**11**(4):959–75.
12. Moral-Muñoz JA, Herrera-Viedma E, Santisteban-Espejo A, Cobo MJ. Software tools for conducting bibliometric analysis in science: an up-to-date review. *Profesional de la información [Internet]* 2020;**29**(1):1699–2407 [cited 2022 Dec 6], Available from: https://revista.profesionaldelainformacion.com/index.php/EPI/article/view/epi.2020.ene.03.
13. Falagas ME, Pitsouni EI, Malietzis GA, Pappas G. Comparison of PubMed, Scopus, Web of science, and google scholar: strengths and weaknesses. *Faseb J [Internet]* 2008;**22**(2):338–42. Available from: https://onlinelibrary.wiley.com/doi/full/10.1096/fj.07-9492LSF.
14. van Eck NJ, Waltman L. Visualizing bibliometric networks. *Measuring Scholarly Impact [Internet]* 2014:285–320 [cited 2022 Dec 6], Available from: https://link.springer.com/chapter/10.1007/978-3-319-10377-8_13.
15. Wang H, Liu F, Ma H, Yin H, Wang P, Bai B, et al. Associations between depression, nutrition, and outcomes among individuals with coronary artery disease. *Nutrition* 2021;**86**:111157.
16. Aydinoglu AU, Taskin Z, Chen C. The citespace manual. *College of Computing and Informatics [Internet]* 2014 [cited 2022 Dec 6], Available from: https://www.researchgate.net/profile/Arsev-Aydinoglu-2/publication/274377526_Collaborative_interdisciplinary_astrobiology_research_a_bibliometric_study_of_the_NASA_Astrobiology_Institute/links/5670463b08ae0d8b0cc0e112/Collaborative-interdisciplinary-astrobiology-research-a-bibliometric-study-of-the-NASA-Astrobiology-Institute.pdf.
17. van Eck NJ, Waltman L. Software survey: VOSviewer, a computer program for bibliometric mapping. *Scientometrics [Internet]* 2009;**84**(2):523–38 [cited 2022 Dec 7], Available from: https://akjournals.com/view/journals/11192/84/2/article-p523.xml.
18. Abhishek Srivastava M. Mapping the influence of influencer marketing: a bibliometric analysis. *Market Intell Plann* 2021;**39**(7):979–1003.
19. Hernández-Vásquez A, Alarcon-Ruiz CA, Bendezu-Quispe G, Comandé D, Rosselli D. A bibliometric analysis of the global research on biosimilars. *J Pharm Policy Pract [Internet]* 2018;**11**(1):1–8. Mar 27 [cited 2023 Jan 7];Available from: https://joppp.biomedcentral.com/articles/10.1186/s40545-018-0133-2.
20. Agarwal A, Durairajanayagam D, Tatagari S, Esteves SC, Harlev A, Henkel R, et al. Bibliometrics: tracking research impact by selecting the appropriate metrics. *Asian J Androl [Internet]* 2016;**18**(2):296 [cited 2023 Jan 7];/pmc/articles/PMC4770502/.
21. Ballew BS. *Elsevier's Scopus® Database* 2009;**6**(3):245–52. 101080/15424060903167252 [cited 2023 Jan 7], Available from: https://www.tandfonline.com/doi/abs/10.1080/15424060903167252.
22. Bozorgmehr K, Saint VA, Tinnemann P. The "global health" education framework: a conceptual guide for monitoring, evaluation and practice. *Glob Health [Internet]* 2011;**7**(1):1–12 [cited 2023 Jan 13], Available from: https://link.springer.com/articles/10.1186/1744-8603-7-8.
23. Klein MD, Kahn RS, Baker RC, Fink EE, Parrish DS, White DC. Training in social determinants of health in primary care: does it change resident behavior? *Acad Pediatr* 2011;**11**(5):387–93.
24. Sills MR, Hall M, Colvin JD, Macy ML, Cutler GJ, Bettenhausen JL, et al. Association of social determinants with children's hospitals' preventable readmissions performance. *JAMA Pediatr [Internet]* 2016;**170**(4):350–8 [cited 2023 Jan 13], Available from: https://jamanetwork.com/journals/jamapediatrics/fullarticle/2491662.
25. Mangold KA, Bartell TR, Doobay-Persaud AA, Adler MD, Sheehan KM. Expert consensus on inclusion of the social determinants of health in undergraduate medical education curricula. *Acad Med [Internet]* 2019;**94**(9):1355–60 [cited 2023 Jan 13], Available from: https://journals.lww.com/academicmedicine/Fulltext/2019/09000/Expert_Consensus_on_Inclusion_of_the_Social.30.aspx.
26. Dharamsi S, Espinoza N, Cramer C, Amin M, Bainbridge L, Poole G. Nurturing social responsibility through community service-learning. *Lessons learned from a pilot project* 2010;**32**(11):905–11. 103109/01421590903434169 [cited

2023 Jan 13], Available from: https://www.tandfonline.com/doi/abs/10.3109/01421590903434169.
27. Wolff JL, Spillman BC, Freedman VA, Kasper JD. A national profile of family and unpaid caregivers who assist older adults with health care activities. *JAMA Intern Med [Internet]* 2016;**176**(3):372–9 [cited 2023 Jan 13], Available from: https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2491683.
28. Beck AF, Henize AW, Kahn RS, Reiber KL, Young JJ, Klein MD. Forging a pediatric primary care–community partnership to support food-insecure families. *Pediatrics [Internet]* 2014;**134**(2):e564–71 [cited 2023 Jan 13].
29. Sartorius BKD, Sartorius K. Global infant mortality trends and attributable determinants - an ecological study using data from 192 countries for the period 1990-2011. *Popul Health Metr [Internet]* 2014;**12**(1):1–15 [cited 2023 Jan 13], Available from: https://link.springer.com/articles/10.1186/s12963-014-0029-6.
30. Gonzalo JD, Haidet P, Papp KK, Wolpaw DR, Moser E, Wittenstein RD, et al. Educating for the 21st-century health care system: an interdependent framework of basic, clinical, and systems sciences. *Acad Med [Internet]* 2017;**92**(1):35–9 [cited 2023 Jan 13], Available from: https://journals.lww.com/academicmedicine/Fulltext/2017/01000/Educating_for_the_21st_Century_Health_Care_System_.16.aspx.
31. Knight SE, van Wyk JM, Mahomed S. Teaching research: a programme to develop research capacity in undergraduate medical students at the University of KwaZulu-Natal, South Africa. *BMC Med Educ [Internet]* 2016;**16**(1): 1–8 [cited 2023 Jan 13], Available from: https://link.springer.com/articles/10.1186/s12909-016-0567-7.
32. O'Brien MJ, Garland JM, Murphy KM, Shuman SJ, Whitaker RC, Larson SC. Training medical students in the social determinants of health: the Health Scholars Program at Puentes de Salud. *Adv Med Educ Pract [Internet]* 2014;**5**:307 [cited 2023 Jan 14];Available from:/pmc/articles/PMC4178477/.
33. Harden RM. International medical education and future directions: a global perspective. *Academic Medicine [Internet]* 2006;**81**(12 SUPPL) [cited 2023 Jan 9], Available from: https://journals.lww.com/academicmedicine/Fulltext/2006/12001/International_Medical_Education_and_Future.5.aspx.
34. Bindler RC, Richardson B, Daratha K, Wordell D. Interdisciplinary health science research collaboration: strengths, challenges, and case example. *Appl Nurs Res* 2012;**5**(2):95–100.
35. Lewis JH, Lage OG, Kay Grant B, Rajasekaran SK, Gemeda M, Like RC, et al. Addressing the social determinants of health in undergraduate medical education curricula: a survey report. *Adv Med Educ Pract* 2020;**11**:369–77.

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Original Research

Lifestyle behaviour patterns in the prevention of type 2 diabetes mellitus: the Fukushima Health Database 2015–2020

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ABSTRACT

Objectives: Lifestyle behaviours associated with the incidence of type 2 diabetes mellitus (T2DM) need further clarification using health insurance data.
Study design: This is a cohort study.
Methods: In 2015, 193,246 participants aged 40–74 years attended the specific health checkups and were observed up to 2020 in Fukushima, Japan. Using the principal component analysis, we identified two patterns from ten lifestyle behaviour questions, namely, the “diet–smoking” pattern (including smoking, alcohol drinking, skipping breakfast, eating fast, late dinner, and snacking) and the “physical activity–sleep” pattern (including physical exercise, walking equivalent activity, walking fast, and sufficient sleep). Then, individual pattern scores were calculated; the higher the scores, the healthier the behaviours.
Results: The accumulative incidence rate of T2DM was 630.5 in men and 391.9 in women per 100,000 person-years in an average of 4 years of follow-up. Adjusted for the demographic and cardiometabolic factors at the baseline, the hazard ratio (95% confidence interval) of the highest versus lowest quartile scores of the “diet–smoking” pattern for T2DM risk was 0.82 (0.72, 0.92; *P* for trend = 0.002) in men and 0.87 (0.76, 1·00; *P* for trend = 0.034) in women; that of the “physical activity–sleep” pattern was 0.92 (0.82, 1·04; *P* for trend = 0.0996) in men and 0.92 (0.80, 1·06; *P* for trend = 0.372) in women. The “physical activity–sleep” pattern showed a significant inverse association in non-overweight men.
Conclusions: Lifestyle behaviour associated with a healthy diet and lack of smoking may significantly lower the risk of T2DM in middle-aged Japanese adults.

Introduction

Life expectancy is reduced by 4–10 years in people with diabetes aged 40–60 years, with an increased risk of mortality due to cardiovascular and renal diseases as well as cancer.[1] Type 2 diabetes, a disease characterised by insulin resistance, is more closely related to lifestyle than genetic factors. It differs from type 1 diabetes, a disease in which the immune system mistakenly destroys the insulin-producing beta cells in the pancreas. Risk factors for type 2 diabetes mellitus (T2DM), such as cardiovascular diseases and obesity, are multifaceted and interrelated.[1,2] Therefore, promoting healthy behaviours, such as eating reduced-calorie meals and exercising more, is the fundamental strategy to reduce the risk of developing T2DM.

The American Diabetes Association recommends that individuals with pre-diabetes undergo an intensive behavioural lifestyle intervention program, including consuming low-calorie foods or receiving pharmacologic therapy, if needed, to achieve and maintain loss of initial body weight to prevent T2DM.[3] In 2008, the Japanese government issued a new health policy that included

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detailed annual health checkups and specific counselling (health promotion guidance) for all beneficiaries aged 40–74 years, targeting individuals with metabolic syndrome risk.[4] Consequently, adults with pre-diabetes and abdominal obesity benefited from the national health programme.[5–7] Furthermore, community-based randomised trials using healthcare resources also reported that a lifestyle intervention program reduces the incidence of T2DM-impaired glucose tolerance,[8,9] suggesting that lifestyle intervention for T2DM risk may be more effective than drug treatment.[10]

Many studies on lifestyle behaviours were conducted either on single factors,[11–14] or in the scenarios of combining risk factors such as Breslow's scores,[15] Life Simple 7,[16] Life Essential 8,[17] lifestyle index,[18] and behaviour classes[19] in measuring the associations with T2DM incidence risk. Breslow's score evaluates the combined risk of lifestyle factors such as alcohol consumption, smoking, exercise, skipping breakfast, sleep, and body weight and has been used in studies on T2DM globally since 2013. A Japanese study showed that participants who scored $\geq$3 points had a 0.69–0.31-times lower risk than those who scored 1–2 points.[15] The American Heart Association implemented the health promotion of Life's Simple 7 goal in 2010.[16] A cohort study revealed that participants who achieved at least two of Life's Simple 7 goals had a lower risk of diabetes than those meeting one or none of these components.[20] In 2022, Life's Essential 8 was issued with a new scoring algorithm comprising diet, physical activity, nicotine exposure, body mass index (BMI), blood lipids, blood glucose, and blood pressure adopted from Life's Simple 7, as well as sleep health.[17] A systematic review indicated that individuals with the healthiest lifestyle had a 75% lower risk of T2DM incidence than those with the least-heathy lifestyle.[21]

Japan has achieved universal health coverage since the 1960s. To improve the health policy for T2DM prevention, it is recommended to integrate and analyse the available databases to estimate the T2DM burden as well as the impact of lifestyle intervention on T2DM risk.[1] However, few studies revealed T2DM risk concerning combined lifestyle risk profiles or overall patterns among the Japanese populations. Thus, this study aimed to examine the associations between lifestyle behavioural patterns identified by the Specific Health Checkup variables and T2DM incidence.

Methods

Study population

The Fukushima Health Database includes data from annual health checkups and health insurance claims of the National Health Insurance as well as part of the Employee Health Insurance (small-to-medium-sized enterprises). In this study, we retrieved data for all participants aged 40–74 years who attended at least one health checkup in 2015 or had claims data in follow-up years between 2016 and 2020.

Demographic and lifestyle behaviour

Demographic data included age, sex, and residential area. The self-administered questionnaires comprised 22 items on medical history, alcohol consumption, smoking, physical activity, and dietary habits/behaviour, and the participant responses to the questionnaires were used to determine the lifestyle behaviour patterns, which reflected an individual's current behavioural profiles (a total of ten questions).

Clinical examinations

Measurements of BMI (kg/m^2, defined as body weight divided by body height square), waist circumference (cm), fasting blood glucose (mg/dL), low-density lipoprotein cholesterol (LDL-C, mg/dL), high-density lipoprotein cholesterol (HDL-C, mg/dL), triglyceride (mg/dL), systolic blood pressure (SBP, mmHg), and diastolic blood pressure (DBP, mmHg) were recorded. Abnormalities of these conditions were defined as fasting blood glucose level being $\geq$126 mg/dL, SBP $\geq$140 mmHg, DBP $\geq$90 mmHg, LDL-C $\geq$140 mg/dL, HDL-C <40 mg/dL, or triglyceride $\geq$150 mg/dL.

Ascertainment of incident type 2 diabetes

Information on T2DM occurrence, including medical, diagnostic procedure combination, and dispensing receipts, was identified from the database. We considered inpatient and outpatient receipts confirmed based on the International Classification of Diseases 10th revision E11-E14 and pharmaceutical classification 396 (antidiabetic agent).

Statistical analysis

A total of 291,649 residents attended health checkups in 2015 (Fig. 1). We included 204,014 individuals in this study, excluding those with T2DM and history of stroke, heart disease, and renal disease reported in 2015, and those who did not attend all health checkups or did not have claim data available during 2016 and 2020. After excluding those with four or more missing answers (1% men and 3% women) to the behaviour questions, 193,246 participants were included in the analysis.

In coding the ten risk factors selected, we assigned ascending numbers along weak risk categories, for example, “1” for “no” and “2” for “yes” in answering the question “Do you have sufficient sleep for rest?”: “1” for “faster,” “2” for “normal,” and “3” for “slower” in answering the question “How fast do you eat compared with others?” Then, in the analysis dataset, we imputed these missing values of behaviour variables and clinical measurements of blood pressure, glucose, and cholesterol as per sex, using the median value from available answers, respectively.[22] In this way, the validity of the results was not affected.

Because lifestyle behaviour variables in the health checkup questionnaire were categorical, we calculated the polychoric correlation coefficients for each pair.[23] Based on the polychoric correlation coefficients of lifestyle factors, the behavioural patterns (latent variables) were derived using the principal component analysis (PCA). The varimax rotation of the identified patterns was applied to improve their interpretability. We selected two factors mainly according to eigenvalues (>1.5), scree plots, and factor interpretability and considered factors with absolute loadings of $\geq$0.3 to account for each component.[24] Among four factors that satisfied the criteria, a two-factor solution appeared to describe the most meaningfully distinctive behaviour patterns of the study population. The cumulative variance explained by the two factors was 0.39 in men and 0.41 in women. We labelled the derived patterns as the “diet–smoking” pattern (including smoking, alcohol drinking, skipping breakfast, eating fast, late dinner, and snacking) and the “physical activity–sleep” pattern (including physical exercise, walking equivalent activity, walking fast, and sufficient sleep) based on question items with high factor loadings, i.e., more conjugated behaviour variables, in each pattern. To reflect how closely behaviour resembles each identified pattern, we calculated the pattern-specific scores for each study participant based on the combinations of behaviours given by the standardised scoring coefficients.[23,25] For further analysis, we categorised the behaviour pattern scores into quartiles (Q1–Q4).

We used the Cox regression model to estimate the associations between behavioural patterns and the incidence of new-onset T2DM in the follow-up years between 2016 and 2020. We calculated the person-year by the onset date of outpatient or inpatient

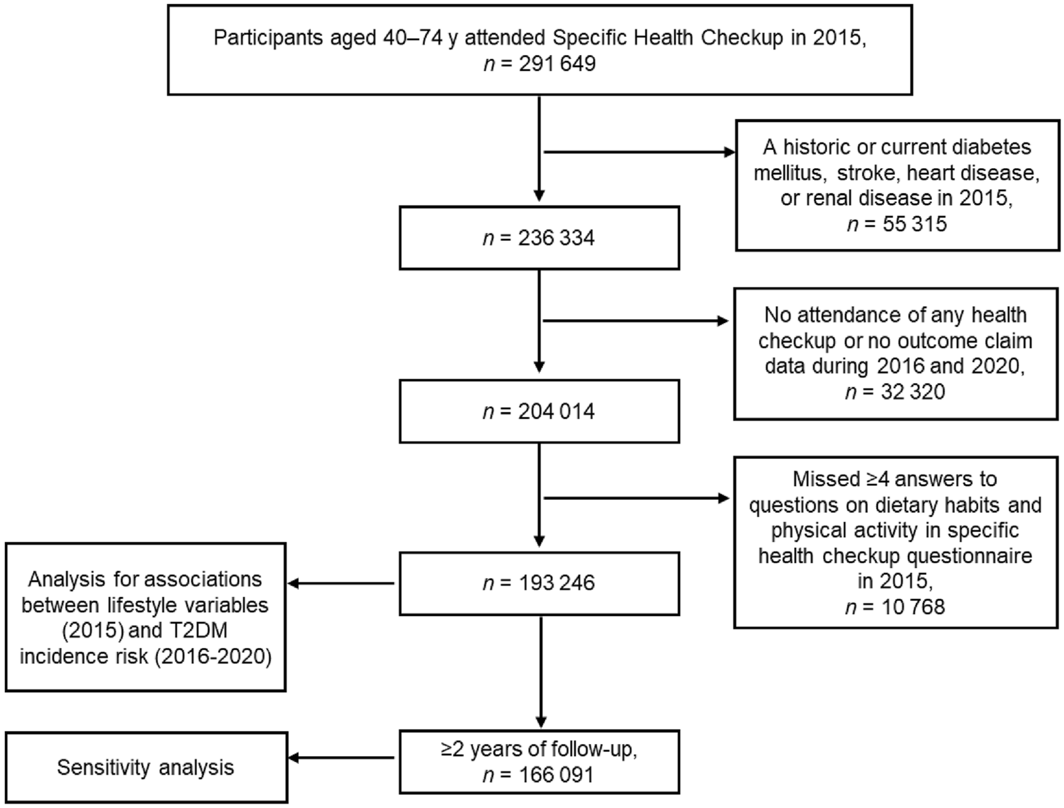

Fig. 1. Data flow for analysis, Fukushima Health Database 2015–2020.

(date on which they get admitted to the hospital or take drugs repeatedly), whichever came first, and if no death date, the last health checkup date was recorded as the census. Hazard ratios and 95% confidence intervals (95% CI) were estimated using the first quartile of pattern scores as the reference. Multivariable regression analyses were conducted with adjustments for variables according to previous publications on cardiovascular risk factors identified by Fukushima Health Management Surveys.[26–29] Model 1 was adjusted for age and residential area; model 2 further included clinical measurements at the baseline. BMI, waist circumference, SBP, and DBP were in normal distributions. Age was grouped as 40–44, 45–49, 50–54, 55–59, 60–64, 65–69, and 70–74 years; residential areas (home address registry) included Aizu, Nakadori, Hamadori, and Outside Fukushima according to the second medical administrative areas in Fukushima, and fasting blood glucose, LDL-C, HDL-C, and triglycerides were categorised into quartiles. A linear trend was tested using the median value of pattern scores in quartile categories as continuous variables. Because overweight/obesity plays a complex role in T2DM development,[30] we tested the potential interactions between behaviour patterns and BMI; then, we provided a stratified analysis for BMI with a 25 kg/m^2 cut-off.

To better address the association of behaviour patterns with T2DM cases diagnosed late, we conducted a sensitivity analysis excluding participants in the first two years of follow-up. To confirm the study findings, we also performed regression analysis using the dataset by applying ten multiple imputations under the missing at-random assumption to handle the missing values of included variables. All data were separately analysed for men and women due to lifestyle disparity, using SAS statistical software version 9.4 for Windows (SAS Institute, Cary, NC). All P values reported were two-sided, and a P value of <0.05 was considered statistically significant.

Results

Table 1 shows the participant characteristics during specific health checkups in 2015. Healthy behaviours were higher in women than in men, i.e., current smoking was 36.1% and 8.8%, eating faster was 29.0% and 24.6%, often skipping breakfast was 17.8% and 9.5%, and everyday alcohol drinking was 47.3% and 11.5% in men and women, respectively. However, women had more snacks between meals but less sufficient sleep than men. Except for LDL-C and HDL-C, clinical measurements recorded for men were higher than those in women.

The mean follow-up was 3.97 years in men and 3·98 years in women. The number (person-years) of new T2DM cases was 2273 (360,501) in men and 1600 (408,233) in women. The accumulative incidence rate of T2DM was 630.5 in men and 391.9 per 100,000 person-years in women.

All paired polychoric correlation coefficients were statistically significant, except those between current smoking and eating fast ($r = -0.0025$, $P = 0.612$) as well as snacking and walking fast ($r = 0.0098$, $P = 0.156$) in men; current smoking and walking fast ($r = 0.0008$, $P = 0.913$), alcohol drinking and sufficient sleep ($r = 0.0081$, $P = 0.096$), alcohol drinking and physical exercise ($r = 0.0069$, $P = 0.154$), late dinner and walking fast ($r = 0.0014$, $P = 0.814$), and eating fast and physical exercise ($r = -0.0005$, $P = 0.915$) in women. Table 2 shows the lifestyle behaviours and factor loadings of two patterns identified. Similar patterns were observed in men and women. In each pattern, healthy behaviour categories, except alcohol drinking, had higher median scores than counterpart categories both in men and women (Supplementary Table 1).

The higher scores of both lifestyle patterns in men and women were significantly associated with T2DM incidence risk during the follow-up years in the age- and area-adjusted model (Table 3). In

Table 1
Characteristics of participants at the baseline, Fukushima Health Database, 2015.

	Men (n = 90 769)		Women (n = 102 477)		P-value
Age (years), mean (SD)	57·5 (10.1)		59·4 (9·7)		<·0001
Lifestyle behaviour question					
Current smoking (yes), %	36·1		8·8		<·0001
Light physical exercise ≥30 min, ≥2 times/week in for more than 1 year (yes), %	28·8		26·7		<·0001
Walking or equivalent activity, ≥1 h/day (yes), %	36·3		34·1		<·0001
Walking faster than those of the same age (yes), %	46·0		42·2		<·0001
Easting faster compared to others, %					<·0001
Faster	29·0		24·6		
Normal	64·4		68·0		
Slower	6·6		7·4		
Late dinner within 2 h before sleep, ≥3 times/week (yes),	30.4		15·8		<·0001
Snacking besides 3 meals, ≥3 times/week (yes), %	11·1		14·4		<·0001
Skipping breakfast, ≥3 times/week (yes), %	17·8		9·5		<·0001
Alcohol drinking, %					<·0001
Every day	47·3		11·5		
Occasionally	25·9		26·4		
Almost no	26·8		62·1		
Sufficient sleep (yes), %	70.8		67·3		<·0001
Clinical measurement					
Body Mass Index (kg/m^2), mean (SD)	23·7	(3·2)	22·6	(3·6)	<·0001
Waist circumference (cm), mean (SD)	84·3	(9·0)	80.4	(9·8)	<·0001
Diastolic blood pressure (mmHg), mean (SD)	78·5	(11·0)	74·0	(10.5)	<·0001
Systolic blood pressure (mmHg), mean (SD)	127·6	(15·6)	123·8	(16·0)	<·0001
Fasting blood glucose (mg/dL), median (interquartile)	94	(91, 102)	93	(88, 98)	<·0001
Low-density lipoprotein cholesterol (mg/dL), mean (SD)	123·4	(31·3)	126·7	(31·1)	<·0001
High-density lipoprotein cholesterol (mg/dL), mean (SD)	57·4	(14·9)	67·0	(15·6)	<·0001
Triglyceride (mg/dL), median (interquartile)	105	(74, 154)	83	(61, 115)	<·0001

SD, standard deviation.

model 2, significant inverse associations and linear trends were observed in the “diet–smoking” pattern (reduced risk 18% in men and 13% in women) but not in the “physical activity–sleep” pattern both in men and women. After the exclusion of participants in the first two years of follow-ups (model 3), significant inverse associations for the “diet–smoking” pattern remained in men (reduced risk by 27%) and women (reduced by 15%).

In addition, when adding the interaction term of pattern score (continuous variable) and BMI (continuous variable), a significant interaction effect was observed in the “diet–smoking” pattern in men (P-interaction = 0.001). In a further stratified analysis, both men and women with overweight/obesity showed inverse associations of “diet–smoking” pattern scores with T2DM incidence risk, whereas only men with BMI <25 kg/m^2 showed an inversed association of “physical activity–sleep” pattern scores with T2DM incidence risk (Table 4).

In the repeated analysis for the dataset with ten multiple imputations, we observed similar regression analysis results, including those in the main effect model and the results in stratified analysis by overweight status (Supplementary Table 2).

Discussion

This study enriched the evidence of combined healthy lifestyle behaviours to prevent the incidence of T2DM, deriving behavioural patterns from a health insurance database. In both men and women, the “diet–smoking” pattern had a prominently inverse association with the incidence of T2DM compared to the “physical activity–sleep” pattern. The “physical activity–sleep” pattern also showed a protective effect on T2DM risk in non-overweight men.

Combined behaviour factors versus behaviour patterns

Focussing on multiple risk factors instead of one certain is the primary priority for reducing the global burden of T2DM.[21] Understandably, the comprehensive evaluation of healthy lifestyle

Table 2
Factor loadings of lifestyle behaviour patterns identified by principal component analysis, Fukushima Health Database, 2015.

Lifestyle behaviour	Men		Women	
	Diet-smoking	Physical activity-sleep	Diet-smoking	Physical activity-sleep
Skipping breakfast, ≥3 times/week	**0.724**	0.159	**0.743**	0.163
Late dinner within 2 h before sleep, ≥3 times/week	**0.689**	0.014	**0.680**	0.055
Current smoking	**0.479**	0.170	**0.689**	0.093
Alcohol drinking	−0.049	−0.064	**0.458**	−0.099
Snacking besides three meals, ≥3 times/week	**0.616**	−0.026	**0.483**	0.140
Eating faster compared to others	0.296	−0.160	0.203	−0.082
Light physical exercise ≥30 min, ≥2 times/week for more than 1 year	0.165	**0.836**	0.152	**0.822**
Walking or equivalent activity, ≥1 h	0.016	**0.835**	−0.048	**0.811**
Walking faster than those of the same ages	−0.101	**0.664**	−0.146	**0.673**
Sufficient sleep	**0.427**	**0.313**	0.274	**0.383**
Scores, median (interquartile)	0.223 (−0.509, 0.677)	−0.142 (−0.844, 0.717)	0.278 (−0.387, 0.634)	−0.081 (−0.799, 0.744)

*Loadings of an absolute value of ≥0.30 are shown in bold.
Abbreviation: SD: standard deviation.

Table 3
Associations between lifestyle behaviour patterns scores and diabetes mellitus incidence risk, Fukushima Health Database, 2015–2020.

	Pattern Scores	Men (n = 90 769)		Women (n = 102 477)	
		HR	95% CI	HR	95% CI
Diet–smoking					
Model 1[a]	Q1 (lowest)	Ref.	–	Ref.	–
	Q2	0.86	(0.77, 0.97)	0.78	(0.67, 0.90)
	Q3	0.81	(0.71, 0.91)	0.82	(0.71, 0.95)
	Q4	0.73	(0.64, 0.82)	0.86	(0.75, 0.99)
	P for trend	<0.001		0.019	
Model 2[b]	Q1 (lowest)	Ref·	–	Ref·	–
	Q2	0.94	(0.84, 1·06)	0.82	(0.71, 0.95)
	Q3	0.90	(0.80, 1·02)	0.85	(0.74, 0.99)
	Q4	0.82	(0.72, 0.92)	0.87	(0.76, 1·00)
	P for trend	0.002		0.034	
Model 3[c]	Q1 (lowest)	Ref·	–	Ref·	–
	Q2	0.92	(0.80, 1·05)	0.83	(0.70, 0.97)
	Q3	0.87	(0.76, 1·00)	0.84	(0.71, 0.99)
	Q4	0.73	(0.63, 0.84)	0.85	(0.73, 1·00)
	P for trend	<0.001		0.033	
Physical activity–sleep					
Model 1[a]	Q1 (lowest)	Ref·	–	Ref·	–
	Q2	1·11	(0.99, 1·24)	0.89	(0.78, 1·02)
	Q3	1·01	(0.92, 1·11)	0.80	(0.69, 0.92)
	Q4	0.88	(0.78, 0.99)	0.79	(0.69, 0.91)
	P for trend	0.004		0.001	
Model 2[b]	Q1 (lowest)	Ref·	–	Ref·	–
	Q2	1·04	(0.92, 1·16)	0.88	(0.77, 1·01)
	Q3	0.98	(0.87, 1·10)	0.87	(0.75, 1·00)
	Q4	0.92	(0.82, 1·04)	0.92	(0.80, 1·06)
	P for trend	0.0996		0.372	
Model 3[c]	Q1 (lowest)	Ref·	–	Ref·	–
	Q2	1·02	(0.89, 1·16)	0.87	(0.74, 1·01)
	Q3	0.99	(0.87, 1·13)	0.86	(0.73, 1·02)
	Q4	0.90	(0.78, 1·03)	0.94	(0.80, 1·10)
	P for trend	0.076		0.665	

HR, hazard ratio; CI, confidence interval.
[a] Model 1: adjusted for age (40–44, 45–49, 50–54, 55–59, 60–64, 65–69, and 70–74) and area (Aizu, Nakadori, Hamadori, and Outside Fukushima).
[b] Model 2: further adjusted for body mass index (kg/m^2), waist circumference (cm), fast blood glucose (mg/dL) (quartile), systolic blood pressure (mmHg), diastolic blood pressure (mmHg), high-density lipoprotein cholesterol (mg/dL) (quartile), low-density lipoprotein cholesterol (mg/dL) (quartile), and triglyceride (mg/dL) (quartile).
[c] Model 3: same as the Model 2 for those in two or more years of follow-up (77 419 men and 88 672 women).

Table 4
Associations between lifestyle patterns scores and diabetes mellitus incidence risk in insured participants overweight or non-overweight, Fukushima Health Database, 2015–2020.

	Pattern Scores	Men, BMI <25 kg/m^2 (n = 62 285)		Men, BMI ≥25 kg/m^2 (n = 28 484)		Women, BMI <25 kg/m^2 (n = 79 963)		Women, BMI ≥25 kg/m^2 (n = 22 514)	
		HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
Diet–smoking									
Model 1[a]	Q1 (lowest)	Ref.	–	Ref.	–	Ref.	–	Ref.	–
	Q2	1·07	(0.88, 1·30)	0.83	(0.71, 0.96)	0.82	(0.66, 1·01)	0.77	(0.63, 0.94)
	Q3	1·08	(0.89, 1·32)	0.71	(0.60, 0.83)	0.95	(0.77, 1·17)	0.74	(0.60, 0.91)
	Q4	0.92	(0.76, 1·24)	0.69	(0.59, 0.81)	0.95	(0.78, 1·16)	0.80	(0.66, 0.96)
	P for trend	0.458		<0.001		0.754		0.006	
Model 2[b]	Q1 (lowest)	Ref·	–					Ref·	–
	Q2	1·07	(0.88, 1·31)	0.90	(0.77, 1·05)	0.83	(0.67, 1·02)	0.84	(0.69, 1·02)
	Q3	1·14	(0.93, 1·38)	0.78	(0.67, 0.92)	0.96	(0.78, 1·18)	0.76	(0.62, 0.94)
	Q4	0.95	(0.78, 1·16)	0.77	(0.65, 0.90)	0.95	(0.78, 1·16)	0.81	(0.67, 0.98)
	P for trend	0.761		0.0004		0.762		0.011	
Physical activity–sleep									
Model 1[a]	Q1 (lowest)	Ref·	–	Ref·	–	Ref·	–	Ref·	–
	Q2	0.95	(0.80, 1·14)	1·14	(0.98, 1·33)	0.95	(0.78, 1·16)	0.85	(0.71, 1·02)
	Q3	0.91	(0.76, 1·08)	1·01	(0.86, 1·18)	0.89	(0.72, 1·09)	0.78	(0.64, 0.96)
	Q4	0.83	(0.70, 0.99)	0.89	(0.76, 1·06)	0.87	(0.72, 1·06)	0.89	(0.73, 1·08)
	P for trend	0.029		0.039		0.152		0.259	
Model 2[b]	Q1 (lowest)	Ref·	–					Ref·	–
	Q2	0.91	(0.76, 1·08)	1·15	(0.98, 1·34)	0.94	(0.77, 1·17)	0.84	(0.70, 1·01)
	Q3	0.89	(0.74, 1·06)	1·07	(0.92, 1·26)	0.91	(0.74, 1·12)	0.84	(0.69, 1·03)
	Q4	0.81	(0.68, 0.97)	1·03	(0.87, 1·22)	0.90	(0.75, 1·10)	0.95	(0.78, 1·15)
	P for trend	0.026		0.922		0.338		0.734	

BMI, body mass index, defined as body weight (kg) divided by the square of body height (m); HR, hazard ratio; CI, confidence interval.
[a] Model 1: adjusted for age (40–44, 45–49, 50–54, 55–59, 60–64, 65–69, and 70–74) and area (Aizu, Nakadori, Hamadori, and Outside Fukushima).
[b] Model 2: further adjusted for body mass index (kg/m^2), waist circumference (cm), fast blood glucose (mg/dL) (quartile), systolic blood pressure (mmHg), diastolic blood pressure (mmHg), high-density lipoprotein cholesterol (mg/dL) (quartile), low-density lipoprotein cholesterol (mg/dL) (quartile), and triglyceride (mg/dL) (quartile).

behaviour is better than that for any single behaviour pattern,[18] which shows inconsistent results. For example, in the Chinese prevention trial in high-risk participants, no difference was found in the intervention effect of a single change in diet or exercise habits.[31] A Japanese study using national health insurance data with the same lifestyle questions showed that habits of exercise and active physical activity were positively associated and fast walking was negatively associated with T2DM incidence.[11] A system review revealed that intensive diet and physical activity behavioural counselling reduced the incidence risk of T2DM in both intermediate and long-term follow-up.[32]

We studied varying behaviours to assess their correlation patterns. The Breslow's score has six behaviour components and BMI, and the Life's Essential 8 has five behaviour components and the measurement of BMI, LDL-C, HDL-C, blood pressure, and fasting blood glucose/hemoglobin A1c. A recent Chinese study showed a T2DM risk profile constructed by five lifestyle factors of sleep duration, physical activity, sedentary behaviour, alcohol drinking, and obesity, as well as five metabolic disorders based on clinical measurements, i.e., insulin resistance, dyslipidemia, hypertension, chronic kidney disease, and hyperuricemia.[33] We applied most clinical measurements of T2DM risk at the baseline for adjustment in the regression analysis because they may also serve as the mediate factors in the complicated mechanism of T2DM development.[34] The combined categories (risk numbers) of behaviour factors may not be precisely reflected correlations among behaviour risks in individuals. Patterns, however, closely match lifestyle habits and resemble the synergistic effects of multiple behaviours in a specific population. As individual pattern scores were calculated, both have negative and positive values; higher scores indicate more closed behaviours congregated. Based on codes for behaviour variables in our study, the higher the pattern scores, the healthier the lifestyle habits.

Disparity of associations in gender and overweight/obese status

The association between combined risk factors may not be equal in higher and lower population.[21] The pathophysiology of T2DM differs between obese and non-obese (lean) individuals.[35] Epidemiological studies have shown that obesity is the most crucial risk factor for T2DM, influencing the development of insulin resistance and disease progress. An American study revealed that associations with T2DM risk were consistent among normal, overweight, and individuals with obesity.[20] Our study showed the inverse association of the “diet–smoking” pattern in men and women with overweight/obesity, which was similar to the study using the Japan Medical Data Centre (JMDC) database in which the national health program prevented or delayed the incidence of T2DM with improvement in obesity among male employees with pre-diabetes.[5] The multi-ethnic study on unhealthy clustered behaviour indicated Asians had an increased risk of T2DM associated with the smoking-risky-drinking-inactive class.[19] Asian people are lean compared to western people; the lean participants might attenuate the impact on the incidence risk, but for overweight or people with obesity, in other words, maintaining optimal body weight through healthy dietary habits is essential.[8]

On the other hand, we observed the protective effect of the “physical activity–sleep” pattern in men with BMI <25 kg/m^2, indicating that physical activity may be more effective than dietary intervention in lean people in lowering T2DM risk. Our study supports that high physical activity/low sitting did not attenuate the risk of T2DM associated with overweight/obesity.[36] As the gender disparity in T2DM risk was reported,[28,30] lifestyle factors might modulate adiponectin levels in the general male population.[37] A previous study did report that a healthy diet in reducing T2DM risk was more remarkable in women.[28] Interactions among physical activity, overweight/obesity, and sex are complex.[30] It can be helpful to elucidate the mechanisms in future studies on how behaviour patterns could prevent the onset of T2DM in individuals with obesity or lean phenotypes and in those with diabetes clustering (insulin resistance or β-cell dysfunction).[35]

Perspectives of the behaviour pattern study

The strength of the current study was that it included a large population in the study area and that the associations were measured through an identified cohort and applied baseline measurements of metabolic risk for adjustment in the regression analysis. The pattern score as the latent variable was a rough indicator. It should be noted that a simplified name for a behaviour pattern does not always accurately capture the full range of input variables that significantly contribute to the variance. Clinical consultations are necessary regarding the behaviour components, i.e., detailed personal preventive activity or strategies in T2DM control. Nevertheless, the behavioural pattern studies on T2DM risk may be promoted further in other countries. For health promotion purposes, the study findings are helpful for counselling or intervention by local health authorities, clinicians, or public health practitioners. Moreover, insurance databases could be served as surveillance tools to monitor individual lifestyle behaviours.

Limitations

One of the limitations of this study is that we only used ten behaviour questions for PCA, which may not be applicable in classifying broad behaviours. Therefore, the results of this study on behavioural patterns might not be generalisable to other countries. For example, Breslow's score considers alcohol-drinking amount (g/day),[15] and Life's Essential 8 has a more detailed Dietary Approaches to Stop Hypertension (DASH) diet score, sleep health time, intensive physical activity time, and smoking categories.[17] Due to a large amount of missing information on alcohol consumption in the dataset, we did not incorporate it in the PCA. More informative variables should be considered in further studies, such as alcohol consumption,[17] dietary scores,[17,28] the strength of physical activity,[17] and sleep duration.[18,38] Second, the average four years of follow-up was not long enough, as if the physical exercise/activity effect, for determining the T2DM risk in this study population. Meanwhile, we only computed the baseline pattern scores and could not clarify whether participants' habits affected the associations measured over the years.[18,39] Third, socioeconomic factors, e.g., educational level, family history of T2DM, family income,[21] and occupation,[40] were not available for adjustment in the regression analysis, which were significant determinants of lifestyle behaviour and health literacy in diabetes.[1]

In summary, although not many components, the patterns of healthy lifestyle behaviours elucidated the remarkable prevention of T2DM among middle-aged Japanese. A more favourable strategy is considering the “diet–smoking” pattern, which helps promote smoke-free and healthy eating behaviour in the high-risk population and reduces obesity and diabetes in the general population. This study method could be applied for the assessment, monitoring, and education of healthy behaviours in a community or among individuals for comprehensive prevention of T2DM. Further studies on lifestyle behaviour patterns elucidating the development of type 2 diabetes with long follow-ups are warranted.

Author Statements

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Ethical approval

This study was approved by the Fukushima Medical University Ethical Review Committee (Generic 2021-169).

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Competing interests

None declared.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.puhe.2023.08.026.

References

1. Chan JCN, Lim LL, Wareham NJ, Shaw JE, Orchard TJ, Zhang P, et al. The Lancet Commission on diabetes: using data to transform diabetes care and patient lives. *Lancet* 2021;**396**:2019–82. https://doi.org/10.1016/S0140-6736(20)32374-6.
2. Duan MJ, Dekker LH, Carrero JJ, Navis G. Using structural equation modeling to untangle pathways of risk factors associated with incident Type 2 diabetes: the lifelines cohort study. *Prev Sci* 2022;**23**:1090–100. https://doi.org/10.1007/s11121-022-01357-5.
3. American Diabetes Association. Prevention or delay of type 2 diabetes: standards of medical care in diabetes – 2019. *Diabetes Care* 2019;**42**:S29–33. https://doi.org/10.2337/dc19-S003.
4. Yamagishi K, Iso H. The criteria for metabolic syndrome and the national health screening and education system in Japan. *Epidemiol Health* 2017;**39**:e2017003. https://doi.org/10.4178/epih.e2017003.
5. Narisada A, Shibata E, Hasegawa T, Wakayama R, Suzuki K. The impact of the National Health Program on diabetes incidence among working-age men with prediabetes: a regression discontinuity analysis of a nation-wide database in Japan. *Diabetes Res Clin Pract* 2022;**189**:109946. https://doi.org/10.1016/j.diabres.2022.109946.
6. Takeuchi Y, Kashiwabara K, Hosoi H, Imai H, Matsuyama Y. Longitudinal effects of a nationwide lifestyle intervention program on cardiometabolic outcomes in Japan: an observational cohort study. *Prev Med* 2020;**141**:106301. https://doi.org/10.1016/j.ypmed.2020.106301.
7. Tsushita K, S Hosler A, Miura K, Ito Y, Fukuda T, Kitamura A, et al. Rationale and descriptive analysis of specific health guidance: the nationwide lifestyle intervention program targeting metabolic syndrome in Japan. *J Atherosclerosis Thromb* 2018;**25**:308–22. https://doi.org/10.5551/jat.42010.
8. Sakane N, Sato J, Tsushita K, Tsujii S, Kotani K, Tsuzaki K, et al. Prevention of type 2 diabetes in a primary healthcare setting: three-year results of lifestyle intervention in Japanese subjects with impaired glucose tolerance. *BMC Publ Health* 2011;**11**:40. https://doi.org/10.1186/1471-2458-11-40.
9. Tuomilehto J, Lindström J, Eriksson JG, Valle TT, Hämäläinen H, Ilanne-Parikka P, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med* 2001;**344**:1343–50. https://doi.org/10.1056/NEJM200105033441801.
10. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med* 2002;**346**:393–403. https://doi.org/10.1056/NEJMoa012512.
11. Iwasaki M, Kudo A, Asahi K, Machii N, Iseki K, Satoh H, et al. Fast walking is a preventive factor against new-onset diabetes mellitus in a large cohort from a Japanese general population. *Sci Rep* 2021;**11**:716. https://doi.org/10.1038/s41598-020-80572-y.
12. Kudo A, Asahi K, Satoh H, Iseki K, Moriyama T, Yamagata K, et al. Fast eating is a strong risk factor for new-onset diabetes among the Japanese general population. *Sci Rep* 2019;**9**:8210. https://doi.org/10.1038/s41598-019-44477-9.
13. Chung YS, Harada KH, Igari K, Ishizuka J, Koizumi A. The incidence of diabetes among the non-diabetic residents in Kawauchi village, Fukushima, who experienced evacuation after the 2011 Fukushima Daiichi nuclear power plant disaster. *Environ Health Prev Med* 2020;**25**:13. https://doi.org/10.1186/s12199-020-00852-x.
14. Ogata E, Asahi K, Yamaguchi S, Iseki K, Sato H, Moriyama T, et al. Low fasting plasma glucose level as a predictor of new-onset diabetes mellitus on a large cohort from a Japanese general population. *Sci Rep* 2018;**8**:13927. https://doi.org/10.1038/s41598-018-31744-4.
15. Tatsumi Y, Ohno Y, Morimoto A, Nishigaki Y, Mizuno S, Watanabe S. Lifestyle and the risk of diabetes mellitus in a Japanese population. *J Behav Med* 2013;**36**:225–33. https://doi.org/10.1007/s10865-012-9427-z.
16. Lloyd-Jones DM, Hong Y, Labarthe D, Mozaffarian D, Appel LJ, Van Horn L, et al. Defining and setting national goals for cardiovascular health promotion and disease reduction: the American Heart Association's strategic Impact Goal through 2020 and beyond. *Circulation* 2010;**121**:586–613. https://doi.org/10.1161/CIRCULATIONAHA.109.192703.
17. Lloyd-Jones DM, Allen NB, Anderson CAM, Black T, Brewer LC, Foraker RE, et al. Life's Essential 8: updating and enhancing the American Heart Association's construct of cardiovascular health: a presidential advisory from the American Heart Association. *Circulation* 2022;**146**:e18–43. https://doi.org/10.1161/CIR.0000000000001078.
18. Kuwahara K, Yamamoto S, Honda T, Nakagawa T, Ishikawa H, Hayashi T, et al. Improving and maintaining healthy lifestyles are associated with a lower risk of diabetes: a large cohort study. *J Diabetes Investig* 2022;**13**:714–24. https://doi.org/10.1111/jdi.13713.
19. Cook WK, Li L, Tam CC, Mulia N, Kerr WC. Associations of clustered health risk behaviors with diabetes and hypertension in White, Black, Hispanic, and Asian American adults. *BMC Publ Health* 2022;**22**:773. https://doi.org/10.1186/s12889-022-12938-y.
20. Fretts AM, Howard BV, McKnight B, Duncan GE, Beresford SA, Mete M, et al. Life's Simple 7 and incidence of diabetes among American Indians: the strong heart family study. *Diabetes Care* 2014;**37**:2240–5. https://doi.org/10.2337/dc13-2267.
21. Zhang Y, Pan XF, Chen J, Xia L, Cao A, Zhang Y, et al. Combined lifestyle factors and risk of incident type 2 diabetes and prognosis among individuals with type 2 diabetes: a systematic review and meta-analysis of prospective cohort studies. *Diabetologia* 2020;**63**:21–33. https://doi.org/10.1007/s00125-019-04985-9.
22. Zhang W, Ohira T, Abe M, Kamiya K, Yamashita S, Yasumura S, et al. Evacuation after the great east Japan earthquake was associated with poor dietary intake: the Fukushima health management survey. *J Epidemiol* 2017;**27**:14–23. https://doi.org/10.1016/j.je.2016.08.002.
23. Carlson JC. Creating meaningful factors from dietary questionnaires. [accessed February 10, 2023].
24. Luger E, Aspalter R, Luger M, Longin R, Rieder A, Dorner TE. Changes of dietary patterns during participation in a web-based weight-reduction programme. *Public Health Nutr* 2016;**19**:1211–21. https://doi.org/10.1017/S1368980015002852.
25. Lin J, Fung TT, Hu FB, Curhan GC. Association of dietary patterns with albuminuria and kidney function decline in older white women: a subgroup analysis from the Nurses' Health Study. *Am J Kidney Dis* 2011;**57**:245–54. https://doi.org/10.1053/j.ajkd.2010.09.027.
26. Ohira T, Nakano H, Nagai M, Yumiya Y, Zhang W, Uemura M, et al. Changes in cardiovascular risk factors after the great East Japan earthquake. *Asia Pac J Public Health* 2017;**29**:47S–55S. https://doi.org/10.1177/1010539517695436.
27. Nagai M, Ohira T, Takahashi H, Nakano H, Sakai A, Hashimoto S, et al. Impact of evacuation on trends in the prevalence, treatment, and control of hypertension before and after a disaster. *J Hypertens* 2018;**36**:924–32. https://doi.org/10.1097/HJH.0000000000001626.
28. Ma E, Ohira T, Hirai H, Okazaki K, Nagao M, Hayashi F, et al. Dietary patterns and new-onset type 2 diabetes mellitus in evacuees after the great East Japan earthquake: a 7-year longitudinal analysis in the Fukushima health management survey. *Nutrients* 2022;**14**. https://doi.org/10.3390/nu14224872.
29. Ohira T, Nakano H, Okazaki K, Hayashi F, Nagao M, Sakai A, et al. Trends in lifestyle-related diseases and their risk factors after the Fukushima Daiichi nuclear power plant accident: results of the comprehensive health check in the Fukushima health management survey. *J Epidemiol* 2022;**32**:S36–46. https://doi.org/10.2188/jea.JE20210386.
30. Huebschmann AG, Huxley RR, Kohrt WM, Zeitler P, Regensteiner JG, Reusch JEB. Sex differences in the burden of type 2 diabetes and cardiovascular risk across the life course. *Diabetologia* 2019;**62**:1761–72. https://doi.org/10.1007/s00125-019-4939-5.
31. Pan XR, Li GW, Hu YH, Wang JX, Yang WY, An ZX, et al. Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. The da Qing IGT and diabetes study. *Diabetes Care* 1997;**20**:537–44. https://doi.org/10.2337/diacare.20.4.537.
32. Lin JS, O'Connor E, Evans CV, Senger CA, Rowland MG, Groom HC. Behavioral counseling to promote a healthy lifestyle in persons with cardiovascular risk factors: a systematic review for the U.S. Preventive Services Task Force. *Ann Intern Med* 2014;**161**:568–78. https://doi.org/10.7326/M14-0130.
33. Ye C, Wang Y, Kong L, Zhao Z, Li M, Xu Y, et al. Comprehensive risk profiles of family history and lifestyle and metabolic risk factors in relation to diabetes: a prospective cohort study. *J Diabetes* 2022;**14**:414–24. https://doi.org/10.1111/1753-0407.13289.
34. Min D, Cho E. Associations among health behaviors, body mass index, hypertension, and diabetes mellitus: a path analysis. *Medicine (Baltim)* 2018;**97**:e10981. https://doi.org/10.1097/MD.0000000000010981.

35. Tanabe H, Masuzaki H, Shimabukuro M. Novel strategies for glycaemic control and preventing diabetic complications applying the clustering-based classification of adult-onset diabetes mellitus: a perspective. *Diabetes Res Clin Pract* 2021;**180**:109067. https://doi.org/10.1016/j.diabres.2021.109067.
36. Nguyen B, Bauman A, Ding D. Incident Type 2 diabetes in a Large Australian cohort study: does physical activity or sitting time alter the risk associated with body mass index? *J Phys Act Health* 2017;**14**:13–9. https://doi.org/10.1123/jpah.2016-0184.
37. Tsukinoki R, Morimoto K, Nakayama K. Association between lifestyle factors and plasma adiponectin levels in Japanese men. *Lipids Health Dis* 2005;**4**:27. https://doi.org/10.1186/1476-511X-4-27.
38. Shan Z, Ma H, Xie M, Yan P, Guo Y, Bao W, et al. Sleep duration and risk of type 2 diabetes: a meta-analysis of prospective studies. *Diabetes Care* 2015;**38**:529–37. https://doi.org/10.2337/dc14-2073.
39. Hu H, Nagahama S, Nanri A, Tomita K, Akter S, Okazaki H, et al. Duration and degree of weight change and risk of incident diabetes: Japan Epidemiology Collaboration on Occupational Health Study. *Prev Med* 2017;**96**:118–23. 10.1016/j.ypmed.2016.12.046.
40. Osaki Y, Kuwahara K, Hu H, Nakagawa T, Yamamoto S, Honda T, et al. Shift work and the onset of type 2 diabetes: results from a large-scale cohort among Japanese workers. *Acta Diabetol* 2021;**58**:1659–64. 10.1007/s00592-021-01770-2.

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Letter to the Editor

Mortality burden due to COVID-19: Years of life lost in Turkey

We read with great interest the research article published in Public Health by Gökler and Metintaş (“Years of potential life lost and productivity costs due to COVID-19 in Turkey: one yearly evaluation”).[1] This study covers relevant calculations of mortality and economic burden using years of life lost (YLL) and years of potential life lost due to COVID-19 in Turkey in the first year of the pandemic from March 11, 2020, to March 10, 2021.

YLL calculation is a component that enumerates mortality losses of disability-adjusted life years. YLL is calculated as described by Wyper et al., which applies standard Global Burden of Disease (GBD) methodology of Institute for Health Metrics and Evaluation by comparing a person's age at the time of death with their residual life expectancy.[2] To calculate YLL, in a concise way, we multiply COVID-19 deaths for an age group for males or females or both sexes with life expectancy years in that age group for sex. The following formula has been used to calculate YLL:

$$YLL = \sum_{i=0}^{n} d_{i,g} * l_i$$

where i is age group in years, $d_{i,g}$ is the number of deaths in age group i among persons with sex g, and l_i is the residual life expectancy in age group i.

In Türkiye, data on COVID-19 deaths have been published on the Web site of Ministry of Health on daily basis. COVID-19 deaths could be traced with the national surveillance system. Also, population data and national life expectancy levels data are published by national statistical office. These data are required for YLL calculation.

Open-source COVID-19 deaths data were not disaggregated at all three levels (i.e. sex, age group, and month) for the whole period from March 2020 to December 2021; therefore, some assumptions had to be made to split the data across age groups and over time, unless it is a real-time data.

With a specific point of view, the authors reported that COVID-19 deaths in 0–4 years age groups for males was 27 and calculated YLL 810 for the age group 0–4 years for males. Under this calculation, life expectancy is 30 years for 0–4 years age group. Following calculated YLL and reported deaths for the age group 0–4 years, YLL per 100,000 for the same age and sex group is 21.5, which means that population size is 627.269 lower than the official data.

To conclude this letter, we would like to propose to recalculate mortality burden with disaggregation by age and sex due to COVID-19 deaths in Türkiye in the first year of the pandemic.

References

1. Gökler ME, Metintaş S. Years of potential life lost and productivity costs due to COVID-19 in Turkey: one yearly evaluation. *Publ Health* 2022;**203**:91–6.
2. Wyper GMA, Assunção RMA, Colzani E, Grant I, Haagsma JA, Lagerweij G, et al. Burden of disease methods: a guide to calculate COVID-19 disability-adjusted life years. *Int J Publ Health* 2021;**66**:619011.

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Short Communication

‘Odds Are: They Win’: a disruptive messaging innovation for challenging harmful products and practices of the gambling industry

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ABSTRACT

Objective: This paper presents an evidence informed rationale for focussing on harmful gambling products and industry practices in public health messaging through the example of a recent innovation called ‘Odds Are: They Win’.
Methods: ‘Odds Are: They Win’ was initially developed through coproduction involving public health professionals and people with lived experience of gambling harms and implemented across a city-region area. A review of relevant evidence was undertaken, upon which the research team reflected to draw out the implications of ‘Odds Are: They Win’ for gambling harms messaging.
Results: Evidence is mounting that safer gambling campaigns framed in terms of individual responsibility are ineffective and can generate stigma. ‘Odds Are: They Win’ presents an alternative focus that is not anti-gambling but raises awareness of industry manipulation of the situational and structural context of gambling. This is in-keeping with historical lessons from the stop smoking field and emerging research in critical health literacy. The latter highlights the potential of education on the social and commercial determinants of health to stimulate behaviour change and collective action.
Conclusion: ‘Odds Are: They Win’ is a potentially disruptive innovation for the gambling harms field. Research is required to robustly evaluate this intervention across diverse criteria, target audiences, and delivery settings.

Introduction

Research is increasingly showing that ‘safer gambling’ campaigns, such as ‘Take Time to Think’, are ineffective at stimulating behaviour change,[1,2] with many commentators urging a rethink of the contents and aims of such campaigns.[3–6] Prior ‘responsible gambling’ campaigns were strongly criticised, from a public health perspective, for contributing to the normalisation of harmful commodity consumption.[7–9] Some public health researchers have highlighted the ambiguous nature of campaign contents, which, they argued, may be strategic, aiming to promote favourable attitudes towards products or the industry rather than educate on harm.[7,10] By framing gambling harms in terms of individual responsibility, the gambling industry's role in facilitating harm, through the development and marketing of harmful products, was silenced; responsibility for harm was, instead, pushed onto consumers.[7–9] At the same time, calls for people to gamble responsibly implied that harms are a matter of individual choice or personality type. A binary distinction was constructed between many people who gamble responsibly and those who do not, who are considered to be deficient or faulty in some way.[11] This can have various consequences, including a tendency to stereotype people who encounter harm (e.g. ‘the problem gambler’), and social stigma.[3,12,13]

Gambling harms campaigners and public health researchers have observed how safer gambling campaigns that attempt to move beyond individual responsibility share weaknesses of responsible gambling campaigns.[3,5,11,14] While some responsibility is afforded to gambling operators to enable safer gambling, this is through self-regulation rather than public policy. Furthermore, a similar binary between people who gamble ‘safely’ and small numbers of vulnerable people is posited, serving to retain much of the responsible gambling framework.[14]

Recent public health commentary on safer gambling campaign taglines has emphasised the practical challenges of shifting conclusively from a focus on individual responsibility. The Australian government has replaced its responsible gambling messages with a set of seven taglines, including ‘Chances are you're about to

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lose', designed to avoid generating stigma.[15] As Marko et al. note[3], this safer gambling campaign continues to frame gambling harms in terms of individual decisions and behaviours. Highlighting historical lessons from counter-industry campaigns in the tobacco field,[16] Marko et al. suggest that a focus on harmful products may be more effective at prompting behaviour change and have positive implications for social stigma:[3] such product- or industry-oriented educational campaigns have, however, been slow to emerge in the gambling harms field.

Here, we review the evidence for shifting away from individual responsibility framings and present a potentially disruptive innovation, called 'Odds Are: They Win'. Disruptive innovations are those that upend conventional ways of thinking, often starting small before displacing established products and services.[17] 'Odds Are: They Win' disruptively breaks from individual responsibility by focussing on harmful industry products and practices, pointing to new avenues for safer gambling campaigns that, we argue, demand further research.

Why shift away from individual responsibility?

Health messaging campaigns framed in terms of individual responsibility require an urgent rethink. While some evidence suggests that such campaigns can prompt behaviour change in certain contexts,[18] experimental studies in gambling frequently find null effects,[1,2,19,20] and studies warn of considerable unintended consequences. In environments that are already saturated with product marketing, promoting responsible consumption may add further cues to consume with some experimental studies, in both the gambling and alcohol harms fields, suggesting that they can increase use of harmful commodity items.[20,21] We have already noted that the binary between responsible/controlled gambling and irresponsible/uncontrolled gambling, which underpins responsible and safer gambling campaigns (see earlier), has been linked to stereotypes and social stigma. People who experience gambling harms appear to internalise this binary such that they view themselves, rather than harmful products, as the source of harm.[3,12,13] This is significant because stigma is a major barrier to help-seeking behaviour.[22] Such binary assumptions may also impact on how individuals who gamble below high-risk thresholds understand their gambling and the harms they experience. Indeed, recent advances in the alcohol harms field warn that binary assumptions in lay understandings of addiction can impede individual problem recognition, even among individuals experiencing considerable harm from their drinking.[23] This is partly due to 'the alcoholic' stereotype, which constitutes an identity threat that alcohol users distance themselves from.[24]

It may be tempting to conclude, given these limitations, that health messaging campaigns should have no role in public health strategy for gambling harms. Yet, recent developments in the field of critical health literacy, as well as historical examples of counter-industry campaigns in the stop smoking field, suggest that an industry-oriented focus may be more effective at prompting reflection and behaviour change. Social marketing campaigns focusing on cigarettes as the source of harm, when implemented as part of a joined-up public health strategy, have been found to contribute to reduced smoking prevalence.[16,25] More recently, public health-framed nutrition interventions have successfully harnessed young people's desire for autonomy and social justice to promote healthy eating through enhanced awareness of manipulative marketing strategies.[26,27] Besides these positive impacts on consumption patterns, moreover, an important consideration is the role of counter-industry education in driving social and political change. Recent studies suggest that education on the social and commercial determinants of health may stimulate collective action[28,29] and secure public support for public health policies, in part by inoculating consumers from industry misinformation.[30] The question, then, is not whether we should invest resources in educational, health messaging campaigns but rather what form such campaigns should take.

Why focus on the gambling industry?

The Betting and Gambling Council (BGC), which represents the gambling industry in the UK, frequently cite prevalence surveys to argue against a national public health strategy for gambling harms due to the relatively small percentage of the population in the 'problem gambling' category: 0.5% of adults in England in one estimate.[31] Existing prevalence surveys have, however, well-recognised weaknesses due in part to a reliance on self-reports of a highly stigmatised addiction and challenges accessing high-risk groups:[32] the Gambling Commission is, for this reason, developing a new survey instrument.

Advances in public health research reveal a continuum of diverse individual and social harms ranging from individual health impacts, which include suicide, to disruption to families, relationships and community cohesion.[33] Seven percent of the UK population may be being harmed by someone else's gambling[31] with a recent needs assessment by Greater Manchester Combined Authority estimating that 1 in 15 local residents are experiencing gambling harms.[34] A Public Health England report, reviewed by the Office of Health Improvement and Disparities in 2023, estimated that the total national social cost of gambling in England is up to £1.27 billion.[31] The bulk of this social cost may be concentrated at the low end and middle of the harms continuum because of the large numbers of 'low-risk' and 'moderate' gamblers.[35]

Taking these considerations into account, it becomes difficult to agree with the longstanding position of the BGC that, alongside universal safer gambling messaging, all that is required are targeted interventions for the minority of people who are severely harmed by their gambling.[7] What is more, the stance jars when we consider that industry profits are disproportionally generated by consumers experiencing harm with one estimate, by Landman Economics, calculating that 20% of online profits accrues from 'problem gamblers'.[36] Extensive effort is expended, by the industry, to shape both situational factors (i.e. the supply and marketing of gambling products) and structural factors (i.e. the products themselves) to entice people in and keep them gambling once they start.[37] Product innovations in online and machine gambling, purposefully designed to promote the establishment of repetitive gambling behaviours, appear to be particularly harmful.[38] Natasha Dow Schüll, whose book 'Addiction by Design' is widely cited in the field, describes how these work through a self-contained environment, referred to as 'The Zone', in which players lose track of time and losses in continuous play.[39] While regulation of the design and supply of these addictive products is urgently required, it is our view that industry manipulation of the situational and structural context of gambling presents opportunities for educational interventions to exploit.

'Odds Are: They Win'

'Odds Are: They Win' is a social marketing campaign launched by the Greater Manchester Combined Authority (GMCA) in October 2022. One of the first of its kind in the UK, the campaign raises awareness of addictive products and harmful industry practices through various formats and media. The campaign was coproduced with a lived experience group called GaMHive, consisting of people with experience of gambling harms, providing advice on contents. GaMHive were presented with various design options after an initial consultation. Echoing academic criticism of safer gambling campaigns, GaMHive were critical of one set of images for resembling gambling advertisements too closely. On GaMHive's advice, a second set was developed that, while still retaining gambling imagery, featured bold and impactful statements on gambling harms and the gambling industry's role in facilitating them. Some GaMHive members believed that exposure to this stronger, industry-oriented focus may have made a difference to their own gambling behaviours:

> *The fundamental message that I needed to hear at 16, 17 years old was that the gambling industry makes 14 billion a year. It doesn't do that by making lots of winners. Ninety-nine percent of the customers lose. The other 1% get their accounts restricted or closed. This is the industry you're up against (GaMHive member, personal communication)*

Example 'Odds Are: They Win' advertisements feature in Fig. 1. The DOWN advertisement features information on the diversity of gambling harms, as this is poorly understood among the public.[40] Down denotes both financial loss and unhappiness. The scratch card image replaced an initial roulette wheel, as GaMHive advised the latter could be triggering. LOSE similarly denotes diverse financial and health-related losses. Information is presented on a particularly harmful product, the Fixed Odds Betting Terminal. The FIXED advertisement features a truism regarding the main purpose of the gambling industry with a view to countering marketing that presents operators as friends of people who gamble. These, and other advertisements were implemented over a three-month pilot period on social media and in diverse physical settings, including Greater Manchester's tram system and coffee shop chains. Service evaluation data revealed considerable reach, including an estimated +1.4 million people across the region.[41]

A disruptive innovation?

We consider 'Odds Are: They Win' to be a potentially disruptive innovation in the gambling harms field, recognising that full 'disruptive' status would require individual responsibility–framed campaigns to be displaced more fully. The UK government recently announced an intention to replace industry-funded safer gambling messaging with independent and robustly evaluated public health messages.[42] We propose that 'Odds Are: They Win' is evaluated, as part of this policy drive, to assess the potential of the tagline to raise awareness of the risks of gambling and associated harms. Interestingly, 'Odds Are: They Win' shares similarities with the Australian government's 'Chances are you're about to lose' tagline, which exhibited the strongest impact of 7 similar taglines on testing:[15] i.e. they both target the information asymmetry that sees many people who gamble overstate the odds of winning.[43] However, the direct reference to the gambling industry (i.e. 'They'), along with the accompanying information on harmful products and practices, ensures 'Odds Are: They Win' breaks more conclusively with individual responsibility framings. The campaign is testament to how lived experience–led knowledge can disrupt established research paradigms.[44]

Key questions for 'Odds Are: They Win's' development pertain to future contents, media types, target groups, and delivery contexts. We would argue in favour of a preventative focus on low-risk and moderate-risk gamblers, as opposed to people who are experiencing severe harm: among the latter group, messages promoting sources of support may be more appropriate, although an important consideration is whether 'Odds Are: They Win's' industry-oriented focus has stigma-related benefits here. Among low-risk and moderate-risk users, with research suggesting that stereotypical notions of 'the problem gambler' can complicate individual problem recognition in a way similar to how 'the alcoholic' stereotype functions in the alcohol field,[45] a research priority is to explore the responses of this group to 'Odds Are: They Win'. Bypassing simplistic binaries that imply that harms are experienced by a small subset of people (as opposed to existing on a broad spectrum),[23] 'Odds Are: They Win' could be more conducive to individual reflection and behaviour change than typical safer gambling campaigns.

'Odds Are: They Win' may also have broader relevance to how gambling harms are talked about in society and help counter strategic industry communications, which include efforts to pit consumers against public health actors.[46] GMCA implemented 'Odds Are: They Win' in public settings to stimulate debate in the public sphere.[41] This has potential implications for gambling narratives, social norms, and policy preferences. Public sphere discussion, prompted by 'Odds Are: They Win', could increase support for public health legislation for addressing gambling harms among people who do not gamble, or among people with positive gambling experiences in the past. 'Odds Are: They Win's' evaluation must, therefore, consider diverse criteria, target groups, and delivery settings. For, there may be positive externalities from the universal provision of information on harmful products and industry practices in markets characterised by major information asymmetry and social cost.

Author statements

Ethical approval

The study received ethical approval from the Institute of Health and Social Care Research Ethics Committee, London South Bank University [ETH2122-0114].

Fig. 1. Examples of 'Odds Are: They Win' advertisements.

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Competing interests

TM, JG, EC, CJ, JE, JW and SS have not previously received research funding from the gambling industry, either directly or indirectly. TM, CJ, JW and SS are public health researchers who are new to gambling research. AM has previously received funding from GambleAware and acted as a paid consultant to the Safer Gambling Campaign Board. JG works for the charity Gambling with Lives that has previously received regulatory settlement money from the Gambling Commission for service development: JG's participation in the research was funded via the NIHR grant. EC and JE's roles in gambling harms reduction at the GMCA are funded by regulatory settlement money from the Gambling Commission as part of the National Strategy to Reduce Gambling Harms.

References

1. Newall PWS, Hayes T, Singmann H, Weiss-Cohen L, Ludvig EA, Walasek L. Evaluation of the 'take time to think' safer gambling message: a randomised, online experimental study. *Behav Public Policy* 2023:1–18.
2. Jacob C, Larkin C, Lawrence J. *Safer gambling messaging project (phase 2): an impact evaluation from the behavioural insights team*. The Behavioural Insights Team; 2021.
3. Marko S, Thomas SL, Pitt H, Daube M. The impact of responsible gambling framing on people with lived experience of gambling harm. *Front Sociol [Internet]* 2023;**8** [cited 2023 Mar 12]; Available from: https://www.frontiersin.org/articles/10.3389/fsoc.2023.1074773.
4. Davies S, Collard S, McNair S, Leak-Smith L. *Exploring alternatives to 'safer gambling' messages*. University of Bristol: Personal Finance Research Centre; 2022.
5. GWL A. *Public health approach and "responsible/safer" gambling*. Gambling With Lives; 2022.
6. Newall PWS, Rockloff M, Hing N, Thorne H, Russell AMT, Browne M, et al. Designing improved safer gambling messages for race and sports betting: what can be learned from other gambling formats and the broader public health literature? *J Gambl Stud* 2023;**39**(2):913–28.
7. van Schalkwyk MC, Maani N, McKee M, Thomas S, Knai C, Petticrew M. "When the Fun Stops, Stop": an analysis of the provenance, framing and evidence of a 'responsible gambling' campaign. *PLoS One* 2021;**16**(8):e0255145.
8. Livingstone C, Rintoul A. Moving on from responsible gambling: a new discourse is needed to prevent and minimise harm from gambling. *Publ Health* 2020;**184**:107–12.
9. Hancock L, Smith G. Critiquing the Reno Model I-IV international influence on regulators and governments (2004–2015) – the distorted reality of "responsible gambling". *Int J Ment Health Addict* 2017;**15**(6):1151–76.
10. Smith W, Atkin C, Roznowski J. Are "drink responsibly" alcohol campaigns strategically ambiguous? *Health Commun [Internet]* 2006;**20**(1) [cited 2023 Mar 23]; Available from: https://pubmed.ncbi.nlm.nih.gov/16813484/.
11. van Schalkwyk MCI, Hawkins B, Petticrew M. The politics and fantasy of the gambling education discourse: an analysis of gambling industry-funded youth education programmes in the United Kingdom. *SSM Popul Health* 2022;**18**: 101122.
12. Miller HE, Thomas SL. The problem with 'responsible gambling': impact of government and industry discourses on feelings of felt and enacted stigma in people who experience problems with gambling. *Addict Res Theory* 2018;**26**: 85–94.
13. Miller HE, Thomas SL, Robinson P. From problem people to addictive products: a qualitative study on rethinking gambling policy from the perspective of lived experience. *Harm Reduct J* 2018;**15**(1):16.
14. Wyllie C, Killick E, Kallman A. A review of gambling harm training materials for healthcare professionals. *Tackl Gambl Stigma [Internet]* 2023. Available from: https://tacklinggamblingstigma.com/wp-content/uploads/2023/04/A-Review-of-Gambling-Healthcare-Training-Tackling-Gambling-Stigma.pdf.
15. Chapman F, Priestly K. *Gambling tagline research phase 2: implementation and market testing*. DSS; 2022.
16. Bayly M, Cotter T, Carrol T. Examining the effectiveness of public education campaigns. In: *Tobacco in Australia: facts and issues*. Melbourne: Cancer Council Victoria; 2019.
17. Schmidt GM, Druehl CT. When is a disruptive innovation disruptive? *J Prod Innov Manag* 2008;**25**(4):347–69.
18. Moss AC, Albery IP. The science of absent evidence: is there such thing as an effective responsible drinking message? *Alcoh Alcoh Oxf* 2018;**53**(1):26–30.
19. Lole L, Li E, Russell AM, Greer N, Thorne H, Hing N. Are sports bettors looking at responsible gambling messages? An eye-tracking study on wagering advertisements. *J Behav Addict* 2019;**8**(3):499–507.
20. Newall PWS, Weiss-Cohen L, Singmann H, Walasek L, Ludvig EA. Impact of the "when the fun stops, stop" gambling message on online gambling behaviour: a randomised, online experimental study. *Lancet Public Health* 2022;**7**(5): e437–46.
21. Moss AC, Albery IP, Dyer KR, Frings D, Humphreys K, Inkelaar T, et al. The effects of responsible drinking messages on attentional allocation and drinking behaviour. *Addict Behav* 2015;**44**:94–101.
22. Quigley L. Gambling disorder and stigma: opportunities for treatment and prevention. *Curr Addict Rep* 2022;**9**(4):410–9.
23. Morris J, Albery IP, Heather N, Moss AC. Continuum beliefs are associated with higher problem recognition than binary beliefs among harmful drinkers without addiction experience. *Addict Behav* 2020;**105**:106292.
24. Morris J, Moss AC, Albery IP, Heather N. The "alcoholic other": harmful drinkers resist problem recognition to manage identity threat. *Addict Behav* 2022;**124**: 107093.
25. Hersey JC, Niederdeppe J, Ng SW, Mowery P, Farrelly M, Messeri P. How state counter-industry campaigns help prime perceptions of tobacco industry practices to promote reductions in youth smoking. *Tob Contr* 2005;**14**(6): 377–83.
26. Bryan CJ, Yeager DS, Hinojosa CP. A values-alignment intervention protects adolescents from the effects of food marketing. *Nat Hum Behav* 2019;**3**(6): 596–603.
27. Bryan CJ, Yeager DS, Hinojosa CP, Chabot A, Bergen H, Kawamura M, et al. Harnessing adolescent values to motivate healthier eating. *Proc Natl Acad Sci USA* 2016;**113**(39):10830–5.
28. Sykes S, Wills J, Popple K. The role of community development in building critical health literacy. *Community Dev J* 2018;**53**(4):751–67.
29. Zhou M, Ramírez AS, Chittamuru D, Schillinger D, Ha S. Testing the effectiveness of narrative messages using critical health communication. *J Commun Healthc* 2023:1–8.
30. Scully M, Brennan E, Durkin S, Dixon H, Wakefield M, Barry CL, et al. Competing with big business: a randomised experiment testing the effects of messages to promote alcohol and sugary drink control policy. *BMC Publ Health* 2017;**17**:945.
31. PHE. *Gambling-related harms evidence review: summary*. Public Health England; 2021.
32. Sturgis P. *An assessment of the accuracy of survey estimates of the prevalence of problem gambling in the United Kingdom*. BeGambleAware; 2020.
33. Wardle H, Reith G, Best D. *Measuring gambling-related harms: a framework for action*. Respons Gambl Strategy Board GambleAware; 2018.
34. Gambling Harms GMCA. *Greater Manchester: strategic needs assessment*. Greater Manchester Combined Authority; 2022.
35. Browne M, Erika L, Rawat V. *Assessing gambling-related harm in Victoria: a public health perspective*. Victorian Responsible Gambling Foundation; 2016.
36. Wardle H, Kolesnikov A, Fiedler I, Critchlow N, Hunt K. Is the economic model of gambling dependent on problem gambling? Evidence from an online survey of regular sports betters in Britain, Int Gambl Stud, Vol. 23, 1.
37. Griffiths M. Fruit machine gambling: the importance of structural characteristics. *J Gambl Stud* 1993;**9**(2):101–20.
38. Delfabbro P, King DL, Browne M, Dowling NA. Do EGMs have a stronger association with problem gambling than racing and Casino table games? Evidence from a decade of Australian prevalence studies. *J Gambl Stud* 2020;**36**(2):499–511.
39. Dow-Schull N. *Addiction by design*. Princeton: Princeton University Press; 2012.
40. Milia, C., Albery, I., Moss, A., Forthcoming. The impact of message framing on problem recognition amongst problem and at-risk gamblers. GambleAware final grant report.
41. GMCA. *"Odds Are: They Win": campaign evaluation* [Internet]. Greater Manchester Combined Authority; 2023 [cited 2023 Jul 26]. Available from: https://greatermanchester-ca.gov.uk/media/7896/odds-are-they-win-campaign-report-summary.pdf.
42. UK Gov. *High stakes: gambling reform for the digital age*. Department for Culture, Media and Sport; 2023. Available from: https://www.gov.uk/government/publications/high-stakes-gambling-reform-for-the-digital-age/high-stakes-gambling-reform-for-the-digital-age.
43. Orgaz C, Estévez A, Matute H. Pathological gamblers are more vulnerable to the illusion of control in a standard associative learning task. *Front Psychol* 2013;**4**:306.
44. Higgins M, Lenette C. *Disrupting the academy with lived experience-led knowledge*. Bristol: Bristol University Press; 2023.
45. Miller H. *Hidden harm: low-risk and moderate-risk gambling*. Victorian Responsible Gambling Foundation; 2017.
46. Madden M, McCambridge J. Alcohol marketing versus public health: david and Goliath? *Glob Health* 2021;**17**(1):45.

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Authors' response

Re: Letter to the Editor of Public Health in response to 'Years of potential life lost and productivity costs due to COVID-19 in Turkey: one yearly evaluation'

We would like to thank you for evaluating our article "Years of potential life lost and productivity costs due to COVID-19 in Turkey: one yearly evaluation". We have carefully reviewed the above points based on the article and data. We thank the authors and your editor for giving us the opportunity to review the data again.

The years of life lost (YLL) formula given by the esteemed letter writers and the formula we used in our article are different. The calculation formula for YLL can be found below in the section on the material and method in our article:

$$YLL = \frac{KCe^{ra}}{(r+\beta)^2}\left[e^{-(r+\beta)(L+a)}[-(r+\beta)(L+a)-1]-e^{-(r+\beta)a}[-(r+\beta)a-1]\right]+\frac{1-K}{r}\left(1-e^{-rL}\right)$$

where a ¼ age of death (years), r ¼ discount rate (usually 3%), b ¼ age-weighting constant (e.g. b ¼ 0.04), K ¼ age-weighting modulation constant (e.g. K ¼ 1), C ¼ adjustment constant for age weights (e.g. C ¼ 0.1658), and L ¼ standard life expectancy at the age of death (years).[1,2]

As can be seen in this formula, the discount rate, age-weighting constant, and adjustment constant are used for age-weighted values. The formula we use is the one used in the Global Borden Disease study, and this formula is preferred in the literature.[1–3] In the formula given by the authors of the letter, YLL are calculated without using a correction factor (x). At this point, we believe that the results we obtained are more realistic. If the calculation were made using the formula given by the authors of the letter, the total number of YLL for men would be 269,128. This value would be 23% higher than the value we calculated (205,177).

In our calculations, the average life expectancy for the 0–4 years age group was set at 75.4 years for males. YLL for this age group and YLL per 100,000 for the same age and sex group are consistent with the male population aged 0–4 years (3,254,719) reported in the official data.[4]

In our study, YPLL was also calculated in the 15- to 64-year-old age group using the method indicated by the author. This should be accepted as an important contribution of our study to the literature. It should be noted that there is no other way to obtain study data other than using the open database of the Ministry of Health. The Ministry of Health does not release data for the time period and age groups individually requested by researchers during the pandemic COVID -19. In this case, the necessary assumptions are made about the database shared by the Ministry of Health with the public. In our study, we do not believe that the burden and cost of COVID-19 by age groups and sex were calculated using the methods accepted in the literature and official data sets and that the data should be reanalyzed as the author claims.

References

1. Impact of the burden of COVID-19 in Italy: results of disability-adjusted life years (DALYs) and productivity loss. *Int J Environ Res Publ Health [Internet]* 2020 Jun 13;**17**(12):4233. Available from: https://www.mdpi.com/1660-4601/17/12/4233.
2. Prüss-Üstün A, Mathers C, Corval_an C, Woodward A. Introduction and methods: assessing the environmental burden of disease at national and local levels. *WHO Environ Burd Dis* 2003. Ser No 1:32–35.
3. Institute for Health Metrics and Evaluation. *GBD results tool*. Seattle: University of Washington; 2018. http://ghdx.healthdata.org/gbd-results-tool. [Accessed 10 April 2020]. 4.
4. *[Internet] The results of address based population registration system, 2020*. TURKSTAT; 2021 [cited 2021 Feb 4]. Available from: https://data.tuik.gov.tr/Bulten/Index?p=The-Results-of-Address-Based-Population-Registration- System-2020-37210.

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Letter to the Editor

Re: Role of confounding factors attributing to the changes in physical activity of students and academic staff of Austrian universities during the COVID-19 lockdown

I read with interest the conclusions of Motevalli et al.[1] recently published online by the journal. The authors have concluded that while all measured sociodemographic variables (including sex, age, body mass index, study level, living area, nationality, and Austrian regions) were significantly associated with the direction of physical activity (PA) changes among the students, only living area and Austrian region were found to be significant indicators of the direction of PA changes in academic staff. The conclusions were drawn based on self-reported online survey data on sociodemographic characteristics and PA sample size provided by 4528 students and 1041 academic staff. However, I am afraid that the results may be influenced by certain confounding factors and a lacuna in the methodology.

We understand that the data collection was done from April to July 2021, when a series of COVID-19 restrictions and measures were implemented in Austria, such as online classes, the closure of non-essential businesses, etc., amongst others. We may infer here that the directives to close fitness centres, public parks, and other infrastructure required to engage in a physically active lifestyle could have played a role in the limitation of PA rather than sociodemographic characteristics. This, compounded by the 'stay-at-home' orders of the government, can make it difficult for the public to continue standard PA patterns. Another factor that might be considered is the link between medical conspiracy beliefs and reluctance to engage in health-protective behaviours.[2] This may be extended to the COVID-19 period regarding PA. Despite the benefits of physical activities on mental and physical health during the lockdown period, high-volume and high-intensity physical activities were not recommended during the pandemic, and moderate-to-high-intensity PA of more than 90 min duration without adequate rest can reduce cellular immunity.[3] Furthermore, the authors have not clarified the inclusion and exclusion criteria regarding the COVID-19 symptoms, as it is likely that either the participants or the family members living in the household testing positive for coronavirus, those on quarantine and self-isolation, and those awaiting results of coronavirus testing could limit their PA. The role of social isolation and loneliness, distress and anger, and loss of part-time income to support studies due to COVID-19 as confounding factors on the PA outcomes could not be ruled out either, as the study design is cross-sectional in nature (my apologies if the questionnaire was misinterpreted, as I could not find the English version and my German language skills are poor). Similarly, I do not see the study collecting the socio-economic status of the participants, as previous work has shown that this characteristic can influence the amount of time spent engaging in PA.[4] Finally, it is quite plausible that remote working and learning can blur the roles of family, work, and home commitments, which could affect the study outcomes.[5] As regression analysis between the variables has not been undertaken, it may not be possible to sort out those sociodemographic variables that indeed had a real impact on PA.

Author statements

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Competing interests

The author has no conflict of interest to disclose.

Author contributions

The author confirms sole responsibility for the conception and design, interpretation of results, and manuscript preparation.

References

1. Motevalli M, Drenowatz C, Wirnitzer KC, Tanous DR, Wirnitzer G, Kirschner W, et al. Changes in physical activity during the COVID-19 lockdown based on the sociodemographic profile of 5569 students and academic staff of Austrian universities. *Publ Health* 2023. https://doi.org/10.1016/j.puhe.2023.04.003. Epub ahead of print. PMCID: PMC10073584.
2. Nelson T, Kagan N, Critchlow C, Hillard A, Hsu A. The danger of misinformation in the COVID-19 crisis. *Mo Med* 2020;**117**(6):510–2. PMID: 33311767; PMCID: PMC7721433.
3. Elovainio M, Hakulinen C, Pulkki-Råback L, Virtanen M, Josefsson K, Jokela M, et al. Contribution of risk factors to excess mortality in isolated and lonely individuals: an analysis of data from the UK Biobank cohort study [published correction appears in Lancet Public Health. 2019 Jun;4(6):e280]. *Lancet Public Health* 2017;**2**(6):e260–6. https://doi.org/10.1016/S2468-2667(17)30075-0.
4. Oliveira-Brochado A, Oliveira-Brochado F, Brito PQ. Effects of personal, social and environmental factors on physical activity behavior among adults. *Rev Port Saúde Pública.* 2010;**28**(1):7–17.
5. Vyas L, Butakhieo N. The impact of working from home during COVID-19 on work and life domains: an exploratory study on Hong Kong. *Policy Design Pract* 2021;**4**(1):59–76. https://doi.org/10.1080/25741292.2020.1863560.

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Review Paper

The economic burden of coronary heart disease in mainland China

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ABSTRACT

Objectives: The aim of this study was to systematically evaluate the current economic burden of coronary heart disease (CHD) in mainland China and provide a reference for the formulation of policies to reduce the economic burden of CHD.
Study design: A systematic literature review was conducted of empirical studies on the economic burden of CHD over the past 20 years.
Methods: PubMed, Web of Science, Embase, China Knowledge Resource Integrated Database and the WANFANG database were comprehensively searched for relevant articles published between 1 January 2000 and 22 December 2021. Content analysis was used to extract the data, and Stata 17.0 software was used for analysis. The median values were used to describe trends.
Results: A total of 35 studies were included in this review. The annual median per-capita hospitalisation expense and the average expense per hospitalisation were $3544.40 ($891.64–$18,371.46) and $5407.34 ($1139.93–$8277.55), respectively. The median ratio on medical consumables expenses, drug expenses, medical examination expenses and treatment expenses were 41.59% (12.40%–63.73%), 26.90% (7.30%–60.00%), 9.45% (1.65%–33.40%) and 10.10% (2.36%–66.00%), respectively. The median per-capita hospitalisation expense in the eastern, central and western regions were $9374.45 ($2056.13–$18,371.46), $4751.5 ($2951.95–$8768.93) and $3251.25 ($891.64–$13,986.38), respectively. The median average expense per hospitalisation in the eastern and central regions were $6177.15 ($1679.15–$8277.55) and $1285.49 ($1239.93–$2197.36), respectively. The median average length of stay in the eastern, central and western regions were 9.3 days, 15.2 days and 16.1 days, respectively.
Conclusions: The economic burden of CHD is more severe in mainland China than in developed countries, especially in terms of the direct economic burden. In terms of the types of direct medical expenses, a proportion of medical examination expenses, treatment expenses and drug expenses were lowest in the eastern region, but medical consumables expenses were the highest in this region. This study provides guidance for the formulation of policies to reduce the economic burden of CHD in mainland China.

Introduction

Coronary heart disease (CHD) is the most common type of cardiovascular disease (CVD),[1] the leading cause of death and disability worldwide and the third leading cause of all deaths in people aged >35 years.[2] Worldwide, the regions with the largest increases in the incidence of cardiac event are Latin America, the Middle East and the Far East, but some regional differences have also been reported.[3] In 2020, an Australian study reported that CHD accounts for nearly half (47%) of CVD-related deaths and was the leading

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cause of CVD-related hospitalisations and the highest disease burden in Australia.[4] Similarly, CHD is also the major cause of death in China.[5] The burden of CHD is increasing rapidly in most low- and middle-income countries and has become a significant public health problem.[6]

It was estimated that there were would be around 11 million patients with CHD in mainland China in 2018; by 2020, the number of patients had increased to 11.39 million.[7] The mortality rates of CHD from 2010 to 2019 showed a continuous upward trend.[8] It is predicted that the incidence and mortality of CHD in China will continue to increase in the next decade.[7] It is estimated that the premature cardiovascular mortality rate in China will reach 11% by 2050, compared with 3% in Western Europe.[9]

Patients with CHD need lifelong medication, and some require the implantation of stents to dilate blood vessels, which is a huge economic burden. The average annual growth rate of inpatient expense for CHD is much higher than the national gross domestic product (GDP) growth rate.[10,11] It was reported that CVD was the major source of healthcare costs in the United States and is expected to reach more than $177 billion by 2040.[12] In the United States, each person with CHD loses an average of $698 due to short-term disability.[13] In Europe, productivity losses associated with CHD amount to €13,953 per person per year.[14] In Indonesia, the percentage of productivity loss due to CHD is estimated to be 8% of GDP per year.[6]

A study of the burden of CVDs in China from 1990 to 2016 showed persistent large differences between provinces in the total burden of CVD and CVD subcategories.[15] A systematic review in 2018 of the economic burden of CVD and hypertension in low- and middle-income countries showed that the expenses per episode for hypertension and generic CVD were moderately homogeneous, ranging between $500 and $1500. CHD and stroke expense estimates were typically higher and more heterogeneous, with most studies reporting monthly treatment expenses between $300 and $1000, and some studies reporting more than $5000 per episode.[16] The current related research mostly focuses on the economic burden of CVD and the treatment expense of CHD. However, few studies have compared the economic burden of CHD in different provinces in mainland China.

This study conducted a systematic literature review of empirical studies over the past 20 years. The purpose was to investigate the cost trends of CHD in mainland China and provide an up-to-date status on the economic burden of CHD in mainland China to provide information to formulate and perfect policies and research objectives in this area.

Methods

This systematic review was registered with the International Prospective Register of Systematic Reviews website (ID CRD42023439150).

Search strategy

The search process was conducted in accordance with the Systematic Reviews and Meta-Analyses 2020 guidelines. Two researchers searched five databases (PubMed, Web of Science, Embase, China Knowledge Resource Integrated Database, and WANFANG) for articles related to the economic burden of CHD in China published between 1 January 2000 and 22 December 2021. The language of the articles was limited to Chinese or English. The search strategies were designed as a combination of Medical Subject Headings.

The keywords used for the literature search were as follows: group 1 included ‘coronary heart disease’, ‘CHD’, ‘coronary artery disease’, ‘cardiovascular disease’ and ‘CVD’; group 2 included ‘economic burden’, ‘disease burden’, ‘burden of disease’, ‘diseases expense’, ‘disease cost’, ‘cost of illness’ and ‘inpatient cost’; and group 3 included ‘China’ and ‘Chinese’.

In addition, the reference lists of the included articles were manually searched for further relevant published research to ensure that all eligible studies were included. This study was based on previously published literature and did not require the approval of an ethics committee.

Study selection

Two reviewers screened the titles and abstracts of the retrieved articles independently based on inclusion and exclusion criteria, and any disagreements were resolved by a third independent reviewer.

The inclusion criteria were as follows: (1) studies reported the direct or indirect expense of CHD or chronic disease; (2) studies clarified the expense time.

The exclusion criteria were as follows: (1) non-original work, such as a summary; (2) clinical report; (3) studies without clear indicators; (4) other inconsistent types of literature, such as conference abstracts, editorials and letters to the editor.

Data extraction

Content analysis was used to extract data. Two reviewers independently extracted data from the full texts. Microsoft Excel software was used to save the data, and Stata 17.0 software was used to visualise the results. The data extracted by each reviewer was quality controlled by the other reviewer. All disagreements or discrepancies regarding study inclusion were resolved following discussion by consensus or consultation with a third independent reviewer. The reviewers first eliminated articles unrelated to the theme by reading the titles and abstracts. After this initial screening, the remaining articles were rescreened through the full-text reading. A literature extraction table was used to extract data from the included articles.

The extracted content included (1) basic information (first author, region, publication year, journal name), (2) source of information (data source, hospital grade, hospital type, data period, sample size, sampling method, estimation method), (3) outcomes of the economic burden (direct economic burden, direct medical expense, direct non-medical expense, indirect burden, per-capita hospitalisation expense, average expense per hospitalisation, length of stay [LOS], the proportion of medical examination expenses, treatment expenses, medical consumables and drug expenses).

Definitions

Economic burden of disease: the monetary embodiment of the economic loss to society and the patient caused by the disease, as well as the resources expended for the prevention and treatment of the disease, including the direct economic burden, indirect economic burden and the intangible burden.

Direct economic burden: medical expenses, travel expenses, meals and so on are paid by the patient for receiving medical care services, including direct medical expenses and direct non-medical expenses.

Direct medical expenses: healthcare expenditures used for treating disease, comprising treatment expenses (outpatient visits, surgeries, ward bed and blood infusions, etc.), medical examination expenses (blood tests, computed tomography [CT], biochemical tests, ultrasonography, magnetic resonance imaging [MRI], digital imaging and pathological examinations), medical consumables expenses and drug expenses and so on.

Direct non-medical expenses: other expenses paid by the patient and accompanying persons in the course of receiving health services, such as nutrition, transportation, travel expenses and the expenses of hiring caregivers.

Indirect economic burden: the economic loss to the patient and society due to illness, disability or premature death. All included studies used the human capital approach to estimate indirect economic burden.

Intangible burden: the economic loss caused by the suffering and anxiety of patients and their relatives due to illness. The intangible burden was too subjective and generally difficult to measure; therefore, this study did not analyse the intangible burden of CHD.

Quality assessment

The quality of the included studies was independently assessed using the Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022).[17] There were 28 items on CHEERS 2022. Items 4, 7, 11 and 12 were not applicable to the included studies (Item 4: Health economic analysis plan; Item 7: Comparators, Describe the interventions or strategies being compared and why chosen; Item 11: Describe what outcomes were used as the measure(s) of benefit(s) and harm(s); Item 12: Describe how outcomes used to capture benefit(s) and harm(s) were measured). Therefore, 24 items were used to evaluate the quality of the included studies. As there was no validated scoring system for the checklist, a qualitative assessment of completeness of reporting by items was performed.[18]

Data analyses

The expenses were converted to US dollars ($) using the Campbell and Cochrane Economics Methods Group Evidence for Policy and Practice Information and Coordination Centre (CCEMG – EPPI-Centre) cost converter, with the target currency (country) set to the United States and the target price year set to 2022. Stata 17.0 software was used to analyse the data. Graphs were used to display the expense data. Direct medical expenses were grouped from geographic location and connected with the median to show the trends. The ratio of specific direct medical expenses was used to describe the hospitalisation expenses structure, including the ratio of medical examination expenses, medical treatment expenses, consumables expenses and drug expenses.

Results

Study selection and features

A total of 7418 studies were initially identified from the database search, of which 3257 were duplicates. Through screening of the titles and abstracts, and rejecting studies where the full text was unavailable, 146 full-text studies were assessed for eligibility. Of these, 111 studies were excluded. Finally, a total of 35 studies were included in this review (Fig. 1).

Fig. 2 shows the distribution of provinces and municipalities investigated in the 35 included studies. The studies covered a total of 14 provinces and cities, including the eastern region, central region and western region of China, divided by the National Development and Reform Commission.[19] Nine studies were in the eastern region, including Beijing, Liaoning and Jiangsu. Six studies were from the central region, including Jilin, Henan and Anhui. Sixteen studies were in the western region, including Shaanxi, Chongqing, Guangxi, Yunnan, Xinjiang and Sichuan. Two studies reported the economic burden of CHD nationwide. There were two cross-province studies, one on the economic burden of CHD in eight cities, including Hangzhou, Hefei, Wuhan, Chengdu, Wuxi, Tongling, Baoji and Shihezi, and the other on Shanxi and Qinghai.

Quality evaluation of included studies

Table 1 shows the quality evaluation results of included studies.[20–54] All studies were reported the items 1, 2, 3, 9, 15, 17, 22, 23, 26 and 28. Seven studies did not report the study population, and only seven studies reported the setting and location. The perspective, discount rate, rationale and description of model, characterising heterogeneity and characterising distributional effects were reported by 16 studies, 7 studies, 8 studies, 20 studies and 22 studies, respectively. Only one study did not report the valuation of outcomes. In total, 23 studies were funded.

Population-level studies

Nine articles (25%) were based on population studies (Table 2).[20–28] The data sources of seven studies were different forms of questionnaires, one from the National Health Service Survey Report and one from the information platform. Seven studies reported the direct economic burden. Eight studies reported the indirect economic burden. The estimation method of direct economic burden was a two-step model and curve fitting method ($\lg y = a + bx$). The estimation method of indirect economic burden was the human capital approach.

There were three studies on Yunnan's economic burden of CHD. Li et al.[20] reported that the per-capita direct/indirect economic burden of CHD in 2007 was $3881.37/$499.28. Li et al.[23] and Le et al.[24] reported the per-capita direct/indirect economic burden of CHD in rural Yunnan in 2015, and the results of both studies were similar. Cui et al.[21] reported that the per-capita direct/indirect economic burden of CHD in cross-regional poor rural areas in 2009 was $1045.16/$320.16. Qin et al.[22] showed that the per-capita direct/indirect economic burden of CHD in cross-regional urban residents in 2011 was $2532.08/$186.20. Wang et al.[25] reported that the total direct/indirect economic burden of CHD in Henan rural areas in 2006 was $766.79 million/$464.78 million. Deng et al.[26] reported that the total direct/indirect economic burden of CHD in Xinjiang Production Corps in 2008 was $61.05 million/$1.60 million. Hu et al.[27] and Zhang et al.[28] reported the national direct medical expenses of CHD in 2003, 2012, 2014, 2016 and 2017, and the results showed that the national direct medical expenses of CHD were increasing over time.

Individual-level studies

Basic characteristics

A total of 26 (75%) individual-level studies[29–54] were included in this review (Table 3). The data sources of 14 (53.85%) studies were medical record systems and 8 (30.77%) studies were hospital information systems, and the data for the remaining studies were from health insurance systems. The cluster sampling method was used in most studies (88.46%). The median sample size of 25 studies was 2149 (range: 129–61,026). The median time span of data collection was 1 year (range: 0.5–6).

Evaluation of economic burden

Fig. 3 shows the time trend of direct medical expenses. The annual median per-capita hospitalisation expense was $3544.40 ($891.64–$18,371.46). The overall median average expense per

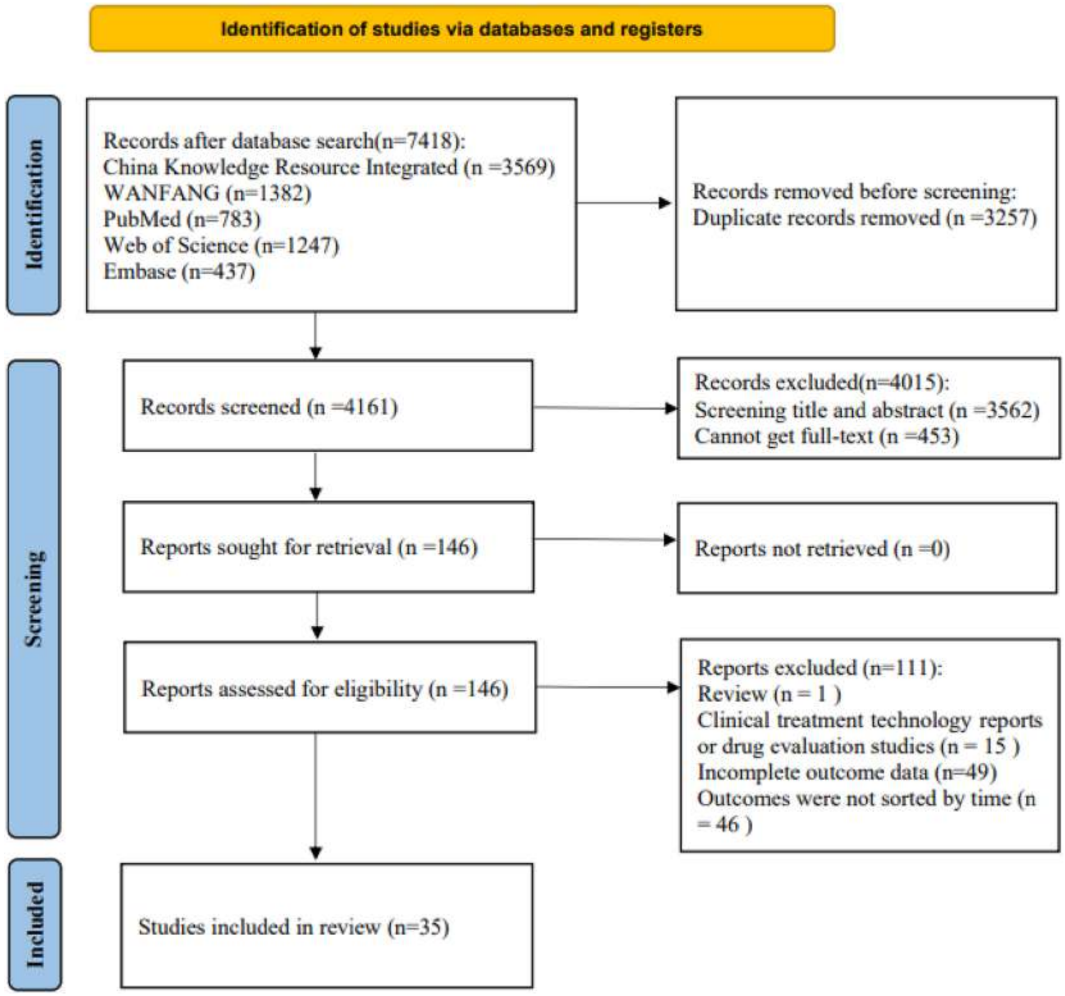

Fig. 1. PRISMA flow diagram for study selection.

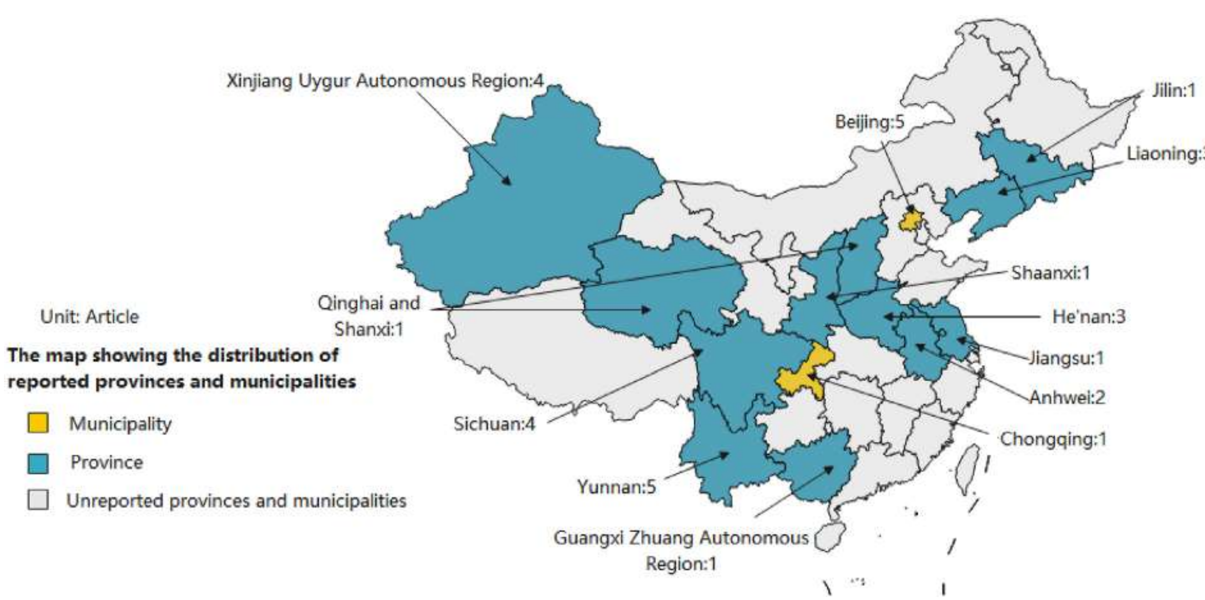

Fig. 2. Distribution map of reported provinces and municipalities.

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Table 1
Quality evaluation results of included studies.[a]

Author	Item 1	2	3	5	6	8	9	10	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
Li L[20]	√	√	√	√	√	√	√	√	√	√	√	–	√	√	√	–	√	√	√	–	√	√	√	√
Cui Y[21]	√	√	√	√	–	–	√	√	√	√	√	–	√	–	√	–	√	√	√	–	–	√	√	√
Qin JM[22]	√	√	√	√	–	–	√	√	√	√	√	–	√	–	–	–	√	√	√	–	√	√	√	√
Li Q[23]	√	√	√	√	√	√	√	√	√	–	√	–	√	√	√	–	√	√	√	–	√	√	√	√
Le C[24]	√	√	√	√	–	–	√	–	√	√	√	√	√	√	√	–	√	√	√	–	√	√	√	√
Wang GJ[25]	√	√	√	√	√	–	√	–	√	√	√	√	√	√	√	–	√	√	√	–	√	√	–	√
Deng DJ[26]	√	√	√	√	–	–	√	√	√	–	√	–	√	–	–	–	√	√	√	–	√	√	√	√
Hu JP[27]	√	√	√	√	–	√	√	√	√	√	√	–	√	√	√	–	√	√	√	–	√	√	–	√
Zhang YH[28]	√	√	√	√	–	–	√	–	√	–	√	–	√	–	–	–	–	√	√	–	√	√	√	√
Xu Y[29]	√	√	√	–	–	√	√	–	√	–	√	√	√	–	–	–	–	√	√	–	√	√	√	√
Yu XH[30]	√	√	√	√	–	–	√	–	√	√	√	–	√	√	√	–	–	√	√	–	√	√	√	√
Zhang Y[31]	√	√	√	√	–	√	√	–	√	–	√	–	√	–	–	–	√	√	√	–	√	√	–	√
Wang Q[32]	√	√	√	√	–	√	√	–	√	√	√	√	√	√	√	–	–	√	√	–	√	√	√	√
Meng NN[33]	√	√	√	√	–	–	√	–	√	–	√	–	√	–	√	–	–	√	√	–	√	√	√	√
Yang YG[34]	√	√	√	√	–	√	√	–	√	–	√	–	√	–	–	–	–	√	√	–	√	√	√	√
Xie L[35]	√	√	√	–	√	√	√	–	√	–	√	–	√	√	√	–	–	√	√	–	√	√	√	√
Zhao X[36]	√	√	√	√	–	√	√	–	√	–	√	√	√	√	√	–	–	√	√	–	√	√	√	√
Xie QX[37]	√	√	√	√	–	–	√	–	√	–	√	√	√	√	√	–	–	√	√	–	√	√	√	√
Wang YL[38]	√	√	√	√	√	√	√	–	√	–	√	√	√	√	√	–	–	√	√	–	√	√	√	√
Ding JM[39]	√	√	√	√	√	√	√	–	√	–	√	–	√	√	√	√	√	√	√	√	√	√	–	√
Wu M[40]	√	√	√	√	–	–	√	–	–	–	√	–	√	–	–	–	–	√	√	–	–	√	√	√
Liu SY[41]	√	√	√	√	–	–	√	–	√	–	√	–	√	√	√	–	–	√	√	–	√	√	–	√
Yu JP[42]	√	√	√	√	√	–	√	–	√	–	√	–	√	–	–	–	–	√	√	–	–	√	√	√
Zhang Q[43]	√	√	√	√	–	–	√	√	√	–	√	–	√	√	√	√	–	√	√	–	√	√	√	√
Zhang P[44]	√	√	√	–	–	–	√	–	√	–	√	–	√	–	–	–	–	√	√	–	–	√	–	√
Zhou LZ[45]	√	√	√	–	–	–	√	–	√	–	√	–	√	√	√	–	–	√	√	–	√	√	√	√
Li ZK[46]	√	√	√	√	–	√	√	–	√	√	√	–	√	√	√	–	–	√	√	–	√	√	√	√
Tao YH[47]	√	√	√	√	–	√	√	–	√	–	√	–	√	√	√	–	–	√	√	–	√	√	√	√
Li YZ[48]	√	√	√	–	–	√	√	–	√	–	√	–	√	–	–	–	–	√	√	–	√	√	–	√
Yang SS[49]	√	√	√	√	–	–	√	–	√	–	√	–	√	–	–	–	–	√	√	–	√	√	√	√
Fan ZJ[50]	√	√	√	√	–	–	√	–	√	–	√	–	√	√	√	–	–	√	√	–	√	√	–	√
Yan JY[51]	√	√	√	–	–	√	√	–	√	–	√	–	√	–	–	–	–	√	√	–	√	√	–	√
Chen NY[52]	√	√	√	–	–	–	√	–	√	√	√	√	√	–	–	–	–	√	√	–	√	√	–	√
Wang J[53]	√	√	√	√	–	–	√	–	√	–	√	–	√	√	√	–	–	√	√	–	√	√	–	√
Yang L[54]	√	√	√	√	–	√	√	–	√	–	√	–	√	√	√	–	–	√	√	–	√	√	–	√

√, reported; "–", not reported.

[a] Item 1: Title, Identify the study as an economic evaluation and specify the interventions being compared. Item 2: Abstract, Provide a structured summary that highlights context, key methods, results and alternative analyses. Item 3: Introduction, Give the context for the study, the study question and its practical relevance for decision-making in policy or practice. Item 5: Study population. Item 6: Setting and location. Item 8: Perspective. Item 9: Time horizon. Item 10: Discount rate. Item 13: Valuation of outcomes. Item 14: Measurement and valuation of resources and costs. Item 15: Currency, price date and conversion. Item 16: Rationale and description of model. Item 17: Analytics and assumptions. Item 18: Characterising heterogeneity. Item 19: Characterising distributional effects. Item 20: Characterising uncertainty. Item 21: Approach to engagement with patients and others affected by the study. Item 22: Study parameters. Item 23: Summary of main results. Item 24: Effect of uncertainty. Item 25: Effect of engagement with patients and others affected by the study. Item 26: Study findings, limitations, generalisability and current knowledge. Item 27: Source of funding. Item 28: Conflicts of interest.

hospitalisation was $5407.34 ($1139.93–$8277.55). The median average LOS was 13.2 days (8.4–30.9).

Fig. 4 shows the proportion of different types of direct medical expenses (note: the years 1997–2002 and 2005–2008 were not reported). Medical consumables and drug expenses were the main direct medical expenses, accounting for 41.59% (12.40%–63.73%) and 26.90% (7.30%–60.00%), respectively. The median proportion of medical examination expenses and treatment expenses was 9.45% (1.65%–33.40%) and 10.10% (2.36%–66.00%), respectively.

There were differences in the per-capita hospitalisation expenses among the eastern, central and western regions (see Fig. 5), with the median expenses being $9374.45 ($2056.13–$18,371.46), $4751.5 ($2951.95–$8768.93) and $3251.25 ($891.64–$13,986.38), respectively. The average expense per hospitalisation was not reported in the western region; however, the median expense per hospitalisation in the eastern and central regions were $6177.15 ($1679.15–$8277.55) and $1285.49 ($1239.93–$2197.36), respectively. The median LOS was 9.3 days (eastern region), 15.2 days (central region) and 16.1 days (western region). Among the different types of direct medical expenses, the median proportion of medical examination expenses in the eastern, central and western regions were 9.45% (6.82%–9.49%), 8.77% (1.65%–33.40%) and 15.28% (5.20%–32.70%), respectively. The median proportion of treatment expenses in the eastern, central and western regions were 3.41% (2.36%–19.00%), 7.15% (6.24%–28.60%) and 12.00% (5.55%–38.31%), respectively. The median proportion of drug expenses in the eastern, central and western regions were 14.46% (7.30%–26.52%), 38.57% (24.61%–45.00%) and 47.12% (7.35%–60.00%), respectively. The median proportion of medical composition expenses in the eastern, central and western regions were 52.82% (40.90%–63.73%), 28.43% (15.65%–41.59%) and 28.47% (12.40%–45.95%), respectively.

Discussion

This review included 35 studies from which data were systematically extracted on study characteristics and expenses of CHD adjusted to 2022 US dollars. This study summarised the economic burden of CHD in China over the past 20 years. In total, 24 of the 35 included studies were published in 2011 and beyond, which indicates that this area of research is gradually attracting attention. This may be directly related to the high incidence, mortality and medical expenses of CHD, as well as the loss of productivity.[1] The present study observed that direct medical expenses were usually

Table 2
Characteristics of population-based research.

Author	Time[a]	Data source	Region	Direct burden ($)	Direct medical expenses ($)	Direct non-medical expenses ($)	Indirect burden ($)	Estimation method[b]
Li L[20]	2007	Questionnaire	Yunnan	3881.37[c]	3585.95[c]	171.91[c]	499.28[c]	M/H
Cui Y[21]	2009	Questionnaire	across regions	1045.16[c]	995.89[c]	49.27[c]	320.16[c]	H
Qin JM[22]	2011	Questionnaire	across regions	2532.08[c]	2475.80[c]	56.28[c]	186.20[c]	M/H
Li Q[23]	2015	Questionnaire	Yunnan	2883.34[c]	2728.10[c]	155.24[c]	103.63[c]	H
Le C[24]	2015	Questionnaire	Yunnan	1411.65[c]	1318.48[c]	93.17[c]	37.63[c]	H
Wang GJ[25]	2006	Questionnaire	Henan	766.79 million[d]	–	–	464.78 million[d]	C/H
Deng DJ[26]	2008	Questionnaire	Xinjiang	61.05 million[d]	57.06 million[d]	3.99million[d]	1.60 million[d]	M/H
Hu JP[27]	2003	Health Service Survey Report	Nationwide	–	14800.86 million[d]	–	16002.28 million[d]	M/H
Zhang YH[28]	2012	Information platform	Nationwide	–	29488.79 million[d]	–	–	M
Zhang YH[28]	2014	Information platform	Nationwide	–	32931.69 million[d]	–	–	M
Zhang YH[28]	2016	Information platform	Nationwide	–	44456.87 million[d]	–	–	M
Zhang YH[28]	2017	Information platform	Nationwide	–	45377.30 million[d]	–	–	M

–, not mentioned.
[a] The time of economic burden.
[b] Estimation method: H = the estimation method of indirect economic burden was human capital approach; M = the estimation method of direct economic burden was two-step model; C = the estimation method of direct economic burden was curve fitting method (lgy = a + bx).
[c] Average.
[d] Total.

Table 3
Characteristics of individual-based research.

Author	Year[a]	Data source	Region	Sampling method	Sample size	Time span (year)	Hospital grade	Index
Xu Y[29]	2021	HIS	Beijing	Cluster	66,647	4	–	Per-capita
Yu XH[30]	2021	Records	Jilin	Stratified cluster	30,953	1	Tertiary	Per-capita
Zhang Y[31]	2019	Records	Liaoning	Cluster	2149	1	–	Per-capita
Wang Q[32]	2019	Records	Liaoning	Cluster	4635	1	Primary	Per-capita
Meng NN[33]	2018	Insurance	Anhui	Random cluster	9307	0.5	–	Every
Yang YG[34]	2018	HIS	Henan	Random	187	–	Tertiary	Per-capita
Xie L[35]	2018	Insurance	Anhui	Random cluster	3365	4	–	Every
Zhao X[36]	2017	HIS	Beijing	Cluster	610,726	1	Tertiary	Every
Xie QX[37]	2017	Records	Beijing	Cluster	6917	1	Tertiary	Every
Wang YL[38]	2017	Records	Liaoning	Cluster	4528	1	–	Daily/every
Ding JM[39]	2017	Records	Shanxi	Cluster	10,301	1	Tertiary	Per-capita
Wu M[40]	2017	Records	Xinjiang	Cluster	129	1	Tertiary	Per-capita
Liu SY[41]	2017	Records	Sichuan	Cluster	635	2	Tertiary	Daily/Per-capita
Yu JP[42]	2017	Insurance	Sichuan	Stratified cluster	1600	3	–	Per-capita
Zhang Q[43]	2016	HIS	Beijing	Cluster	420,714	6	Secondary/Tertiary	Every
Zhang P[44]	2015	Records	Henan	Cluster	1661	1	Tertiary	Per-capita
Zhou LZ[45]	2015	HIS	Sichuan	Cluster	1272	1	Tertiary	Per-capita
Li ZK[46]	2015	HIS	Xinjiang	Cluster	994	1	Secondary	Per-capita
Tao YH[47]	2015	Insurance	Jiangsu	Cluster	6035	1	–	Per-capita
Li YZ[48]	2015	HIS	Chongqing	Cluster	–	5	Tertiary	Per-capita
Yang SS[49]	2009	Records	Yunnan	Cluster	422	5	–	Per-capita
Fan ZJ[50]	2009	Records	Beijing	Cluster	3620	6	Tertiary	Per-capita
Yan JY[51]	2006	HIS	Xinjiang	Stratified cluster	1845	2	–	Per-capita
Chen NY[52]	2005	Records	Guangxi	Stratified random	1393	5	–	Per-capita
Wang J[53]	2003	Records	Yunnan	Cluster	179	1	Tertiary	Per-capita
Yang L[54]	2000	Records	Sichuan	Stratified random	221	1	–	Per-capita

"–", not mentioned; daily, average daily hospitalisation expenses; every, average expenses per hospitalisation; HIS, hospital information system; insurance, health insurance system; Records, medical records system; Per-capita, per-capita hospitalisation expenses.
[a] The year of publication.

the main study indicator, whereas direct non-medical expenses and indirect economic burdens were less frequently reported. The present study also showed that there were differences in the direct medical expenses of CHD in different regions.

The evaluated data on the economic burden of CHD at the population level were relatively scattered. The present review included nine studies based on population-level data, but only two studies were national studies,[27,28] and other studies[20–26] focussed on Yunnan, Henan and other provinces. This study observed that the years of economic burden reported were not consecutive; thus, it was difficult to form a complete report of the economic burden of CHD or establish a forecasting model. It is therefore urgent to increase the investment in scientific research in this field of study to guide more population-level economic burden evaluations and provide reference for decision-making of population interventions in the prevention and control of CHD. For example, cohort studies should be established, which can evaluate the direct economic burden and also the indirect economic burden, especially the impact on productivity.

An Australian study[1] comprehensively assessed and predicted the economic burden of CHD and found that if CHD can be prevented, the total expenses can be reduced by US$14.8 billion. Currently, a study in Australia[2] has constructed a dynamic life table model, which is stratified according to the status of CHD and monitors its direct and indirect economic burden.

In terms of the types of expenses covered by the economic burden, it is more common to study a single direct medical expense.[20–28] It is suggested that more attention should be paid to

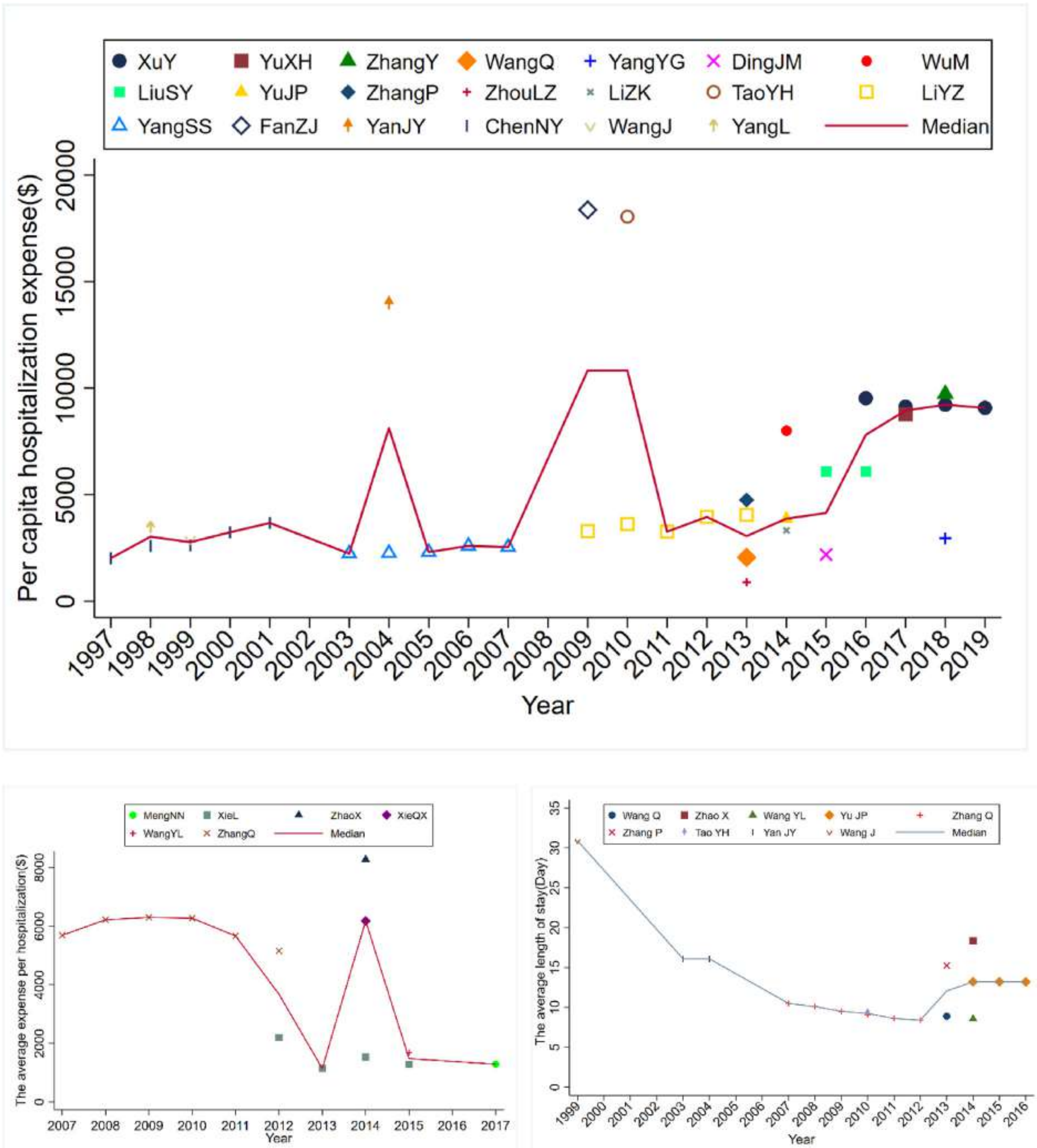

Fig. 3. Time trend of direct medical expenses in individual-level studies.

direct non-medical expenses and the indirect economic burden of CHD in the future.[55] Due to the difficulty of measuring the intangible burden of CHD and there only being a few studies on this content, the present review did not summarise the intangible burden.

The present study found an upward trend in direct medical expenses nationwide, which might be related to the development of medical care and the economy.[56] However, this result is only based on two national studies;[27,28] thus, further research is required to confirm this trend.

Most of the studies at the individual level have focussed on the past 8 years. Data from these studies were obtained from medical institutions, which might lead to some restrictions on the generalisability and usefulness of recommendations provided to decision-makers.[57] The population assessed in these studies was dominated by hospitalised patients with CHD; therefore, individuals who were unable or unwilling to receive treatment were not included.[58,59]

The results found that per-capita hospitalisation expense showed a gradual upward trend from 1997 to 2019. Data on the average expense per hospitalisation were less available. The results showed that the average expense per hospitalisation did not change significantly from 2007 to 2011 but changed significantly from 2011 to 2015, peaking in 2014. However, because these studies were fragmentary, more research is needed to confirm this finding.

The average LOS is an important index to evaluate the utilisation and effect of medical resources.[60,61] This study found that the average LOS showed a gradual downward trend overall, but it

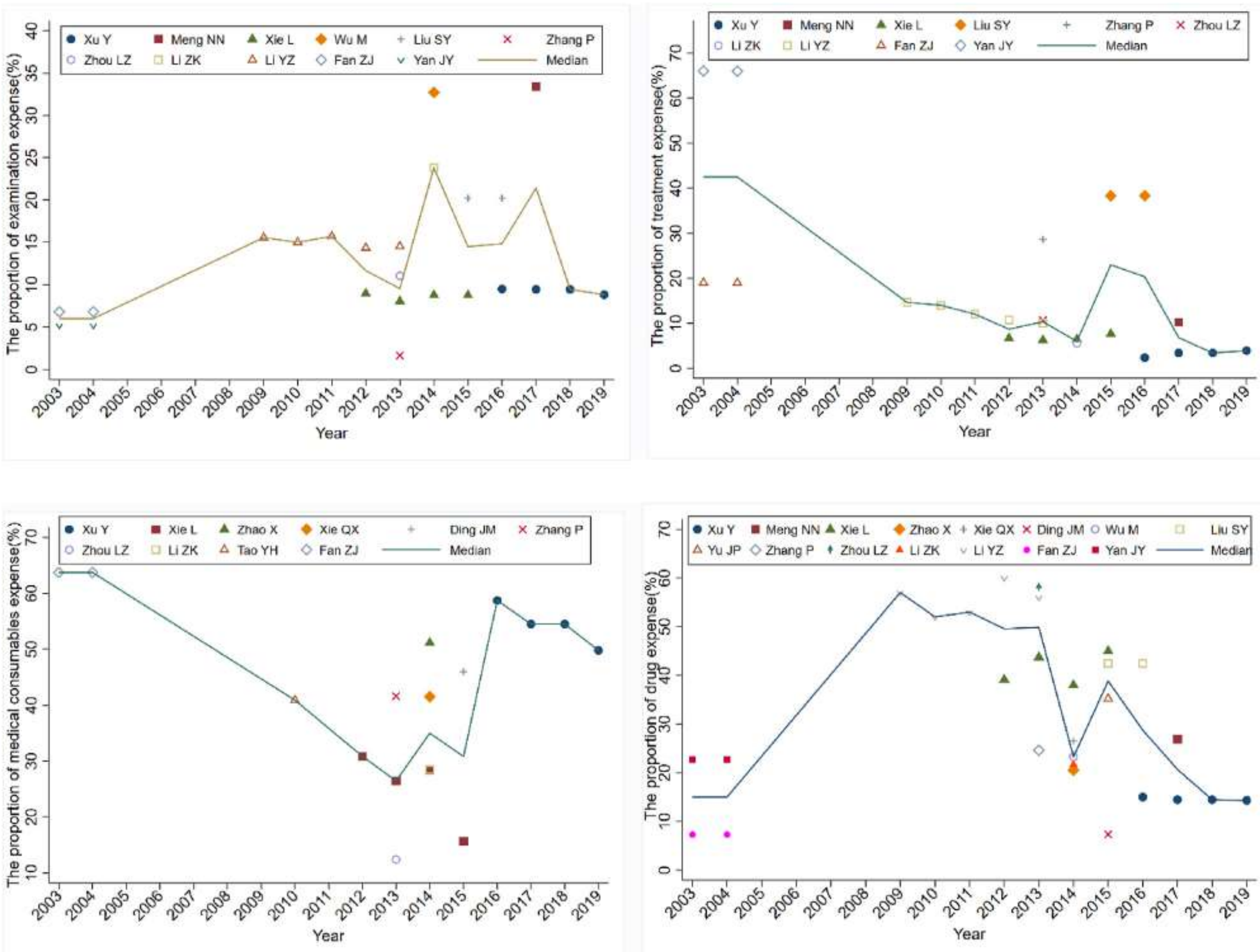

Fig. 4. Proportion of different types of direct medical expense in individual-level studies.

increased slightly from 2013 to 2014 and then stabilised. LOS was longest in 1999, which may be related to the level of medical care provided at this time. Since 2010, the trend in LOS was consistent with the trend of per-capita hospitalisation expenses. This result is similar to several other studies that have shown a positive correlation between hospitalisation expenses and LOS.[62,63]

It was reported that the per-capita hospitalisation expense of CHD in France[64] was about $1559.36, that in Germany[65] was approximately $1607.72 and that in Canada[66] was approximately $1763.41. A French cohort study[67] reported that the mean LOS of myocardial infarction (the most severe type of CHD) was approximately 7 days. However, the present study found that the per-capita hospitalisation expense of CHD in mainland China was approximately $3544.40, and the mean LOS was approximately 13.2 days. Moreover, a Canadian study[66] in 2010 reported the direct economic burden of CHD as $2.2 billion, whereas the economic burden of CHD in mainland China in 2003 was $14.8 billion. It can be seen that the economic burden of CHD in mainland China is very heavy, especially the direct economic burden.

It was found that the expense of drugs as a proportion of total costs has fallen significantly in recent years. The main cause of this might be the elimination of drug markups and the no-price difference system of drug sales in public hospitals in mainland China during the healthcare reform.[68] However, these policies cannot fundamentally address the high cost of health care for patients.[69] This study also found that while the proportion of drug expenses had been somewhat controlled, the proportion of medical consumables expenses had increased. It has been argued that some hospitals have increased the expense of medical consumables to compensate for the decrease in revenue after the abolition of the drug markup.

The expenses for treatment might also fluctuate as healthcare policy-makers have been adjusting healthcare services in recent years.[70] This theory is corroborated by the present review, which showed a decreasing and fluctuating trend in the proportion of treatment costs.

This study also found that the proportion of medical examination expenses to total medical expenses showed an upward trend from 2003 to 2011, a fluctuating trend from 2012 to 2017, and a levelling off after a decline in 2018. The reasons for the fluctuation and downward trend might be related to the continuous adjusting of healthcare service policies and the improvement of healthcare standards. In addition, it is strongly recommended that hospitals control excessive medical examinations to achieve proper and efficient medical care.[71]

There were differences in the direct medical expenses between regions of different economic levels. We found that direct medical expenses for individuals with CHD were higher in the eastern region than in the central and western regions. Meanwhile, the LOS in the western regions was significantly longer than in the central and eastern regions. The difference in direct economic burden of CHD between the eastern, central and western regions might be related

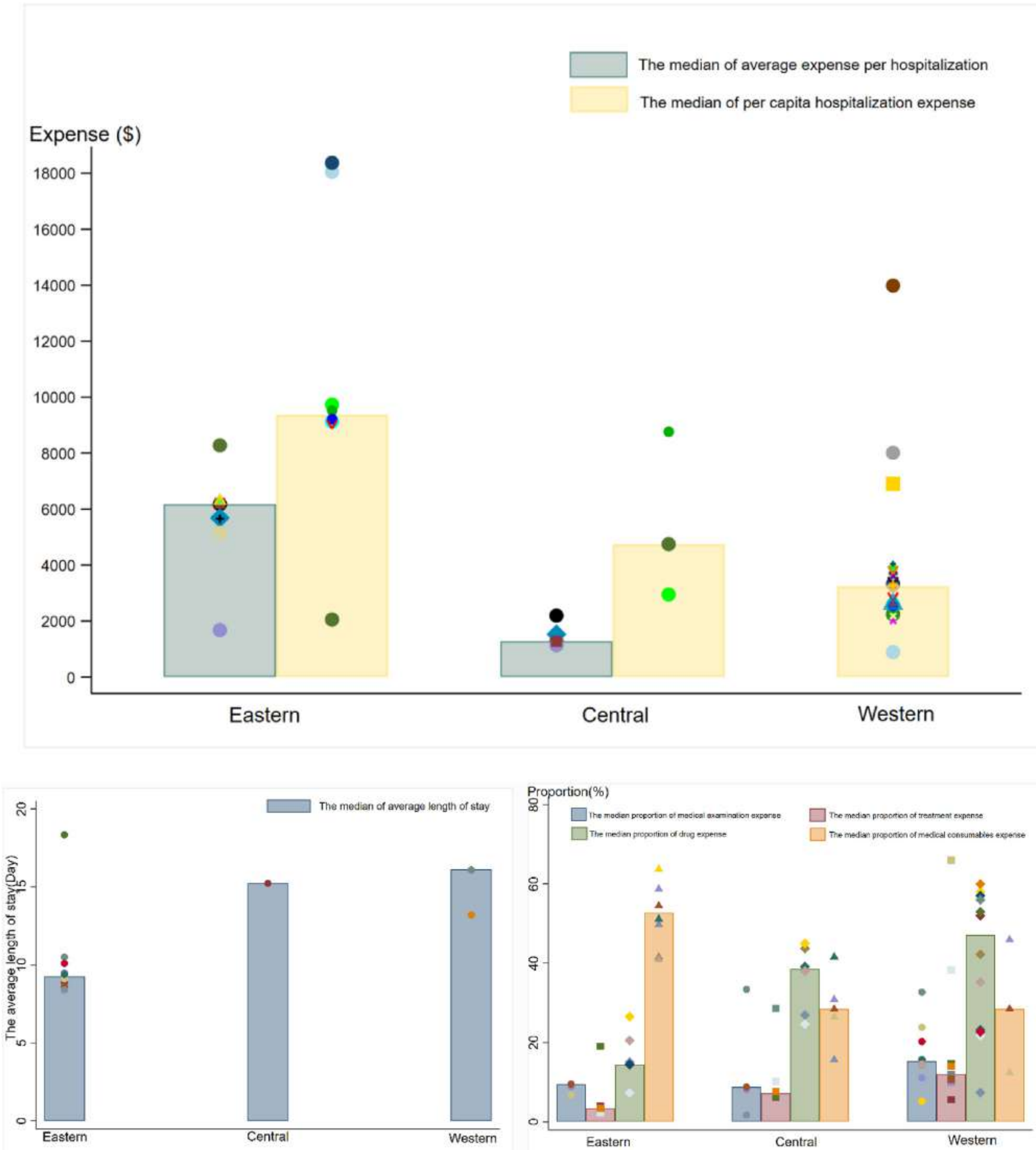

Fig. 5. Direct medical expenses in different regions in individual-level studies.

to the higher income levels and the level of medical technology available in the eastern region. A US study showed that people with high economic levels were at higher risk of suffering from CHD than those with low economic levels.[72]

Among the different types of direct medical expenses, the proportion of medical examination expenses, treatment expenses and medicine expenses were higher in the western region than in the eastern and central regions, which might increase the economic burden for people with CHD in the western regions.[73] However, the proportion of medical consumables expenses was highest in the eastern region, followed by the western and central regions. These results may be due to the lack of medical resources and the levels of treatment available in western regions.

Overall, the Chinese government has worked to reduce the economic burden of CHD in recent years, but with limited effects. Primary healthcare providers are not well placed to share the medical pressure of tertiary care, as patients tend to seek care at tertiary institutions, which also explains the severe economic burden of CHD in mainland China.[71] The following measures are recommended to reduce the economic burden of CHD. First, it is necessary to focus on the importance of preventing CHD based on the individual level, such as smoking cessation programmes, blood pressure control and cholesterol reduction therapies. Savira et al.[1] reported that the values for a preventing 10% reduction of new CHD cases might be A$2.2 increase by $1.59 billion of GDP gained. Second, attention must be paid to prevention strategies at the population level, such as promoting a healthy diet, environmental changes and community-level initiatives (e.g. increasing green space and recreational space). The European Guidelines on Prevention emphasise that small changes in the risk of disease across the whole community lead to a more significant reduction in disease burden than a large change in high-risk groups alone.[74] It is necessary to strengthen the role of the community and primary healthcare institutions in the prevention of CHD. Finally, health systems should insist on health financing reform, which will mobilise additional funding, and strengthen the role of prepaid contributions, effective pooling and strategic purchasing.

Limitations

Although this study provides an important reference for the formulation of policies to reduce the economic burden of CHD in mainland China, caution is warranted regarding the magnitude of the findings. Pooling economic estimates from these studies of different quality and in different regions can only indicate the true extent of the burden. However, the limitations of this study should be noted. First, some studies had unmentioned risks, such as quality evaluation, processing of missing data and missing follow-up results. Second, this review did not include unpublished studies and studies that did not use valid and objective evaluation methods, which resulted in some studies potentially being overlooked. In addition, the studies did not include the influence of confounding factors on the study findings, such as the level of hospital, payer, patient and societal factors. Future studies should attempt to overcome these limitations and comprehensively analyse the economic burden of CHD in China using high-quality methods to provide information for national planning and policy-making.

Conclusions

In conclusion, the economic burden of CHD is more severe in mainland China than in developed countries, especially in terms of the direct economic burden. Although the average LOS for people with CHD has levelled off since 2013, it remains longer than in developed countries. Without timely measures or adjustments to the healthcare services policy, it would put enormous economic pressure on patients, impact the productivity of society and even affect the GDP of the whole country. In addition, the eastern region of mainland China has the highest direct medical expenses and the shortest average LOS. In terms of the types of direct medical expenses, the proportion of medical examination expenses, treatment expenses and drug expenses is lowest in the eastern region, but the proportion of medical consumables expenses is highest in this region. It is possible to adapt medical services for the local context.

This study provides guidance for the formulation of policies to reduce the economic burden of CHD in mainland China and also provides a methodological reference for improved research on the economic burden of CHD.

Author statements

Ethical approval

Not required.

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Competing interests

None declared.

Author contributions

Y.M. contributed to the conceptualisation, visualisation, writing – original draft, writing – review & editing, formal analysis and data analysis. Z.X. contributed to the conceptualisation, visualisation, writing – original draft, writing – review & editing, formal analysis and data analysis. S.Q., Y.Y. and J.H. contributed to the formal analysis, data curation and analysis and writing – review & editing. R.K., X.W. and S.L. contributed to conceptualisation, visualisation and writing – review & editing. W.L. and Y.T. contributed to conceptualisation, visualisation, funding acquisition, formal analysis and writing – review & editing.

References

1. Savira F, Wang BH, Kompa AR, Ademi Z, Owen AJ, Liew D, et al. The impact of coronary heart disease prevention on work productivity: a 10-year analysis. *Eur J Prev Cardiol* 2021;**28**(4):418–25. https://doi.org/10.1093/eurjpc/zwaa037. PMID: 33624015.
2. Almarzooq ZI. The cost of coronary heart disease and the promise of prevention. *Eur J Prev Cardiol* 2022;**29**(6):e213–5. https://doi.org/10.1093/eurjpc/zwaa056. PMID: 33623990.
3. Ralapanawa U, Sivakanesan R. Epidemiology and the magnitude of coronary artery disease and acute coronary syndrome: a narrative review. *J Epidemiol Glob Health* 2021;**11**(2):169–77. https://doi.org/10.2991/jegh.k.201217.001.
4. AIHW. *Cardiovascular disease: impact – Australian Institute of Health and Welfare*. 2019. https://www.aihw.gov.au/reports/heart-stroke-vascular-diseases/cardiovascular-health-compendium/contents/impact. [Accessed 14 November 2019].
5. Zhou M, Wang H, Zhu J, Chen W, Wang L, Liu S, et al. Cause-specific mortality for 240 causes in China during 1990–2013: a systematic subnational analysis for the Global Burden of Disease Study 2013. *Lancet* 2016;**387**(10015):251–72. https://doi.org/10.1016/S0140-6736(15)00551-6. Epub 2015 Oct 26. PMID: 26510778.
6. Uli RE, Satyana RPU, Zomer E, Magliano D, Liew D, Ademi Z. Health and productivity burden of coronary heart disease in the working Indonesian population using life-table modelling. *BMJ Open* 2020;**10**(9):e039221. https://doi.org/10.1136/bmjopen-2020-039221.
7. Report on cardiovascular health and disease in China. Overview of report on cardiovascular health and disease in China 2021. *Chin J Cardiovasc Res* 2022;**20**(7):577–96. https://doi.org/10.3969/j.issn.1672-5301.2022.07.001.
8. Authoritative release-data 'said' coronary heart disease. *J Pract Cardiovasc Cerebrovasc Dis* 2021;**29**(9):4.
9. Roth GA, Nguyen G, Forouzanfar MH, Mokdad AH, Naghavi M, Murray CJ. Estimates of global and regional premature cardiovascular mortality in 2025. *Circulation* 2015;**132**(13):1270–82. https://doi.org/10.1161/CIRCULATIONAHA.115.016021. PMID: 26408271.
10. Estes C, Anstee QM, Arias-Loste MT, Bantel H, Bellentani S, Caballeria J, et al. Modeling NAFLD disease burden in China, France, Germany, Italy, Japan, Spain, United Kingdom, and United States for the period 2016–2030. *J Hepatol* 2018;**69**(4):896–904. https://doi.org/10.1016/j.jhep.2018.05.036. Epub 2018 Jun 8. PMID: 29886156.
11. Schofield D, Cunich M, Shrestha R, Passey M, Veerman L, Tanton R, et al. The indirect costs of ischemic heart disease through lost productive life years for Australia from 2015 to 2030: results from a microsimulation model. *BMC Publ Health* 2019;**19**(1):802. https://doi.org/10.1186/s12889-019-7086-5. PMID: 31226965; PMCID: PMC6588908.
12. Duggan JP, Peters AS, Trachiotis GD, Antevil JL. Epidemiology of coronary artery disease. *Surg Clin North Am* 2022;**102**(3):499–516. https://doi.org/10.1016/j.suc.2022.01.007.
13. Song X, Quek RG, Gandra SR, Cappell KA, Fowler R, Cong Z. Productivity loss and indirect costs associated with cardiovascular events and related clinical procedures. *BMC Health Serv Res* 2015;**15**:245. https://doi.org/10.1186/s12913-015-0925-x.
14. Kotseva K, Gerlier L, Sidelnikov E, Kutikova L, Lamotte M, Amarenco P, et al. Patient and caregiver productivity loss and indirect costs associated with

cardiovascular events in Europe. *Eur J Prev Cardiol* 2019;**26**(11):1150–7. https://doi.org/10.1177/2047487319834770.
15. Liu S, Li Y, Zeng X, Wang H, Yin P, Wang L, et al. Burden of cardiovascular diseases in China, 1990–2016: findings from the 2016 global burden of disease study. *JAMA Cardiol* 2019;**4**(4):342–52. https://doi.org/10.1001/jamacardio.2019.0295. PMID: 30865215; PMCID: PMC6484795.
16. Gheorghe A, Griffiths U, Murphy A, Legido-Quigley H, Lamptey P, Perel P, et al. The economic burden of cardiovascular disease and hypertension in low- and middle-income countries: a systematic review. *BMC Publ Health* 2018;**18**(1): 975. https://doi.org/10.1186/s12889-018-5806-x. PMID: 30081871; PMCID: PMC6090747.
17. Husereau D, Drummond M, Augustovski F, de Bekker-Grob E, Briggs AH, Carswell C, et al. Consolidated health economic evaluation reporting standards 2022 (CHEERS 2022) statement: updated reporting guidance for health economic evaluations. *Value Health* 2022;**25**(1):3–9. https://doi.org/10.1016/j.jval.2021.11.1351.
18. Husereau D, Drummond M, Petrou S, Carswell C, Moher D, Greenberg D, et al. Consolidated health economic evaluation reporting standards (CHEERS) – explanation and elaboration: a report of the ISPOR Health Economic Evaluation Publication Guidelines Good Reporting Practices Task Force. *Value Health* 2013;**16**(2):231–50. https://doi.org/10.1016/j.jval.2013.02.002.
19. Lai HB, Wang GX. Differences of innovation efficiency among central, eastern and western in China from the perspective of industrial agglomeration of electronic and telecommunication equipment manufacturing. *Sci Technol Prog Policy* 2022;**39**(11):52–62. https://doi.org/10.6049/kjjbydc.2021100406.
20. Li L, Cai L, Yang M, Tao J, Zhao K. Study on the economic burden of coronary heart disease in a rural area of Li, Yunnan Province. *Chin Health Econ* 2009;**28**(11):25–6.
21. Cui Y, Liu JA, Ye JL, Wang Q, Yang L, Shi S, et al. Studying the economic burden of rural poors with hypertension and its comorbidities. *Chin Health Serv Manag* 2011;**28**(3):217–218+226.
22. Qin JM, Zhang YC, Zhang LF, Ran DS, Mao L, Wang LK, et al. Prevalence of non-communicable diseases and economic burden of patients in 8 typical cities. *Chin J Public Health* 2014;**30**(1):5–7. https://doi.org/10.11847/zgggws2014-30-01-02.
23. Li Q, Cai L, Wang WL, Li SM, Cui WL, You DY. Analysis of economic burden of four major chronic diseases in rural Yunnan Province. *Chin J Dis Contr Prev* 2016;**20**(9):926–928+944.
24. Le C, Fang Y, Linxiong W, Shulan Z, Golden AR. Economic burden and cost determinants of coronary heart disease in rural southwest China: a multilevel analysis. *Publ Health* 2015;**129**(1):68–73. https://doi.org/10.1016/j.puhe.2014.11.002.
25. Wang GJ, Zhang L, Tian QF, Zhang F, Chen Y. The study of economic burden of rural patients with coronary heart diseases in Henan province. *Med Soc* 2008;(11):35–36+41. https://doi.org/10.3870/YXYSH.2008.11.013.
26. Deng DJ, Wang GJ, Yin TP, Tang JX, Zhang YH, Mao L, et al. Economic burden of non-communicable chronic diseases in Xinjiang production and construction corps. Chin J Publ Health. 26(5):618-620.
27. Hu JP, Rao KQ, Qian JC, Wu J. The study of the economic burden of chronic non-communicable diseases in China. *Chin J Contr Chron Non Commun Dis* 2007;**15**(3):189–93.
28. Zhang YH, Chai P, Zhai TM, Wan Q. Study on accounting and analysis of curative expenditure on cardiovascular diseases in China. *Chin Circ J* 2020;**35**(9):859–65. https://doi.org/10.3969/j.issn.1000-3614.2020.09.003.
29. Xu Y, Liu LM, Cheng W. Research on hospitalization expenses of coronary heart disease based on interrupted time series analysis. *Chin Health Econ* 2021;**40**(9): 53–7.
30. Yu XH, Jiang HR, Jia H, Song FY, Li YY, Zhang JR. Analysis of influencing factors of hospitalization cost of patients with cardiovascular and cerebrovascular diseases in a grade-A tertiary hospital in Jilin province. *Med Soc* 2021;**34**(2): 12–6. https://doi.org/10.13723/j.yxysh.2021.02.003.
31. Zhang Y, Chi WJ, Xu YW, Fu LY. Analysis of influencing factors of hospitalization cost of patients with coronary heart disease based on random forest. *Chin Med Rec* 2019;**20**(2):53–7.
32. Wang Q, Zhang S, Wang Y, Zhang X, Zhang Y. Factors associated with hospitalization costs of coronary heart disease in township hospitals in rural China. *Inquiry* 2019;**56**. https://doi.org/10.1177/0046958019886958.
33. Meng NN, Ding H, Wang HP, Xie T, Yu HY, Yang Q, et al. Analysis of direct inpatient medical expenses and compensation for patients with coronary heart disease in Anhui Province. *Chin Health Resourc* 2018;**21**(6):496–9. https://doi.org/10.13688/j.cnki.chr.2018.18290.
34. Yang YG, Li L, Xu ZW, Qin SY, Shen LJ, Wang Y. Comparison of hospitalization expenses for patients in different hospitals under grading diagnosis and treatment system in Henan province. *Med Soc* 2018;**31**(8):22–30. https://doi.org/10.13723/j.yxysh.2018.08.007.
35. Xie L, Wang HP, Zhou LL, Zhong XX, Ding H. Analysis of the composition and influencing factors of coronary heart disease patients' hospitalization expenses under DRGs in Anhui Province. *Chin J Health Pol* 2018;**11**(5):70–3. https://doi.org/10.3969/j.issn.1674-2982.2018.05.012.
36. Zhao X, Zhang XX, Xie QX, Zhao LY, Jiang Y. Study of the expenses on coronary heart disease in Beijing based on volume data. *Chin Health Econ* 2017;**36**(9): 63–8. https://doi.org/10.7664/CHE20170916.
37. Xie QX, Zhang XX, Zhao Xuan, Zhao LY, Cheng W. Analysis of influencing factors of hospitalization expenses of patients with coronary heart disease in third grade class A hospitals in Beijing city. *Med Soc* 2017;**30**(5):23–5. https://doi.org/10.13723/j.yxysh.2017.05.008.
38. Wang YL, Zhang DL, Zhang YD, Xiang X, Zhang Y. Comparison on the application of multiple statistical models in influencing factors of hospitalization expenses of coronary heart disease. *Chin Health Serv Manage* 2017;**34**(3): 198–200+204.
39. Ding JM, Zhang XZ, Hu XJ, Chen HL, Yu M. Analysis of hospitalization expenditures and influencing factors for inpatients with coronary heart disease in a tier-3 hospital in Xi'an, China: a retrospective study. *Medicine* 2017;**96**(51): e9341. https://doi.org/10.1097/MD.0000000000009341.
40. Wu M, Yu J, Zhang WD, Li YP, Wang GT, Xu T, et al. Analysis the disease constitution and costs of inpatients with circulatory system diseases in Karamay Central Hospital in 2014. *Chin J Evid Based Med* 2017;**17**(8):892–4. https://doi.org/10.7507/1672-2531.201610041.
41. Liu SY, Cao Y, Li Y. Investigation and analysis of hospitalization expenses of five common senile chronic diseases. *Sichuan Med J* 2017;**38**(11):1269–73. https://doi.org/10.16252/j.cnki.issn1004-0501-2017.11.012.
42. Yu JP, Jiang X, Ye Y. Investigation and analysis of drug use in CHD patients from 8 medical institutions in Mianyang area. *China Pharm* 2017;**28**(32):4487–92. https://doi.org/10.6039/j.issn.1001-0408.2017.32.06.
43. Zhang Q, Zhao D, Xie WX, Xie XQ, Wang M, Wang W, et al. Trends in length of hospital stay and in-hospital cost for coronary heart disease from 2007 to 2012 in Beijing. *J Cardiovasc Pulmon Dis* 2016;**35**(2):75–80+105. https://doi.org/10.3969/j.issn.1007-5062.2016.02.001.
44. Zhang P. Influencing factors and survey of 10 kinds of common diseases in medicare patients of a hospital in 2013. *Chin Health Econ* 2015;**34**(8):38–40. https://doi.org/10.7664/CHE20150810.
45. Zhou LZ, Pan M, Tan L, Deng X, Yang S, Zhang M. Comparative analysis of medical service price and disease cost in public hospitals – taking coronary heart disease as an example. *Health Econ Res* 2015;**7**:25–7. https://doi.org/10.14055/j.cnki.33-1056/f.2015.07.006.
46. Li ZK, Wang LH, Pan W, Zhang SY, Yu AP. Hospitalization expenses analysis of different health insurance types of patients with coronary heart disease. *Chin Med Rec* 2015;**16**(12):45–8.
47. Tao YH, Zhang KJ, Chen JR, Wang YQ, Ma YH. Factors influencing hospitalization expenses of chronic disease patients registered with basic medical insurance for urban workers. *Chin Gen Pract* 2015;**18**(7):811–7. https://doi.org/10.3969/j.issn.1007-9572.2015.07.019.
48. Li YZ, Zou P, Shi P. Analysis on disease constitution and fee structure of a hospital in past 5 years. *Chin Med Rec* 2015;**16**(4):58–61.
49. Yang SS, Cai L, Chen ZN, Zhao Y, Wen L. Analysis of medical charge of inpatients with coronary heart disease and influencing factors. *Mod Prev Med* 2009;**36**(3): 461–2.
50. Fan ZJ, Sun GQ, Liang GY, Xu Y. Effects of age and gender on hospitalization cost in patients with coronary artery disease. *Chin J Cardiovasc Res* 2009;**7**(11): 827–32. https://doi.org/10.3969/j.issn.1672-5301.2009.11.011.
51. Yan JY, Huang ZY, Jiang WT, Yan HY, Luo SL, Jia Q. Analysis and study above multiple influence factors in single sort disease costs of inpatients. *Hosp Admin J Chin PLA* 2006;(7):597–9. https://doi.org/10.16770/j.cnki.1008-9985.2006.07.037.
52. Chen NY, Wei B, Meng XY, Liu Y, Feng QM. Analysis and prediction on medical cost of coronary heart disease among urban residents in Guangxi. *Pract Prev Med* 2005;**5**:992–4.
53. Wang J. Multivariate analysis of the hospitalization expenses on coronary atherosclerotic heart disease. *Chin Hosp Manage* 2003;**9**:43–4.
54. Yang L, Mao ZZ, Yan ZM, Kong LZ, Lei ZL. Multifactor analysis of the costs of coronary heart disease patients. *Chin Prev Chron Non Commun Dis* 2000;(2): 60–2.
55. Pan F, Xu W, Li J, Huang Z, Shu Q. Trends in the disease burden of congenital heart disease in China over the past three decades. *Zhejiang Da Xue Xue Bao Yi Xue Ban* 2022;**51**(3):267–77. https://doi.org/10.3724/zdxbxyb-2022-0072.
56. Cai L, Cui W, He J, Wu X. The economic burden of smoking and second hand smoke exposure in rural South-West China. *J Asthma* 2014;**51**(5):515–21. https://doi.org/10.3109/02770903.2014.892964.
57. Kazibwe J, Tran PB, Annerstedt KS. The household financial burden of non-communicable diseases in low- and middle-income countries: a systematic review. *Health Res Policy Syst* 2021;**19**(1):96. https://doi.org/10.1186/s12961-021-00732-y.
58. Lee VWY, Yan BP, Fong TMC, Fung AKP, Cheng FWT. Long-term health-related burden of adult congenital heart diseases in Hong Kong. *J Med Econ* 2019;**22**(8): 814–7. https://doi.org/10.1080/13696998.2019.1613239.
59. Bansilal S, Castellano JM, Fuster V. Global burden of CVD: focus on secondary prevention of cardiovascular disease. *Int J Cardiol* 2015;**201**(Suppl. 1):S1–7. https://doi.org/10.1016/S0167-5273(15)31026-3.
60. Kazemi M, Nazari S, Motamed N, Arsang-Jang S, Fallah R. Prediction of hospitalization length. Quantile regression predicts hospitalization length and its related factors better than available methods. *Ann Ig* 2021;**33**(2):177–88. https://doi.org/10.7416/ai.2021.2423.
61. Goyal V, McPhail SM, Hurley F, Grimwood K, Marchant JM, Masters IB, et al. Cost of hospitalization for bronchiectasis exacerbation in children. *Respirology* 2020;**25**(12):1250–6. https://doi.org/10.1111/resp.13828.
62. Aung YN, Nur AM, Ismail A, Aljunid SM. Determining the cost and length of stay at intensive care units and the factors influencing them in a teaching hospital in Malaysia. *Value Health Reg Issues* 2020;**21**:149–56. https://doi.org/10.1016/j.vhri.2019.09.006.

63. Wang L, Zou H, Ye F, Wang K, Li X, Chen Z, et al. Household financial burden of phenylketonuria and its impact on treatment in China: a crosssectional study. *J Inherit Metab Dis* 2017 May;**40**(3):369–76. https://doi.org/10.1007/s10545-016-9995-0.
64. Bauersachs R, Zeymer U, Brière JB, Marre C, Bowrin K, Huelsebeck M. Burden of Coronary Artery Disease and Peripheral Artery Disease: A Literature Review. *Cardiovasc Ther* 2019 Nov 26;**2019**:8295054. https://doi.org/10.1155/2019/8295054.
65. Smolderen KG, Wang K, de Pouvourville G, Brüggenjürgen B, Röther J, Zeymer U, et al. Two-year vascular hospitalisation rates and associated costs in patients at risk of atherothrombosis in France and Germany: highest burden for peripheral arterial disease. *Eur J Vasc Endovasc Surg* 2012;**43**(2):198–207. https://doi.org/10.1016/j.ejvs.2011.09.016.
66. Smolderen KG, Bell A, Lei Y, Cohen EA, Steg PG, Bhatt DL, et al. One-year costs associated with cardiovascular disease in Canada: insights from the REduction of Atherothrombosis for Continued Health (REACH) registry. *Can J Cardiol* 2010;**26**(8):297–305. https://doi.org/10.1016/s0828-282x(10)70437-2.
67. Blin P, Philippe F, Bouée S, Laurendeau C, Torreton E, Gourmelin J, et al. Outcomes following acute hospitalised myocardial infarction in France: an insurance claims database analysis. *Int J Cardiol* 2016;**219**:387–93. https://doi.org/10.1016/j.ijcard.2016.06.102.
68. Zhu J, Wang W, Wang J, Zhu L. Change in coronary heart disease hospitalisation after chronic disease management: a program policy in China. *Health Policy Plan* 2022:czac101. https://doi.org/10.1093/heapol/czac101.
69. Hsieh MJ, Chiang WC, Sun JT, Chang WT, Chien YC, Wang YC, et al. A prediction model for patients with emergency medical service witnessed out-of-hospital cardiac arrest. *J Formos Med Assoc* 2021;**120**(5):1229–36. https://doi.org/10.1016/j.jfma.2020.09.017.
70. Wang T, Chen L, Yang T, Huang P, Wang L, Zhao L, et al. Congenital heart disease and risk of cardiovascular disease: a meta-analysis of cohort studies. *J Am Heart Assoc* 2019;**8**(10):e012030. https://doi.org/10.1161/JAHA.119.012030.
71. Che X, Li J, Fu W, Fang F. Association between livelihood capital and catastrophic health expenditure among patients with critical illness: a cross-sectional study in rural Shandong, China. *BMJ Open* 2021;**11**(10):e051234. https://doi.org/10.1136/bmjopen-2021-051234.
72. Moran KE, Ommerborn MJ, Blackshear CT, Sims M, Clark CR. Financial stress and risk of coronary heart disease in the Jackson heart study. *Am J Prev Med* 2019;**56**(2):224–31. https://doi.org/10.1016/j.amepre.2018.09.022.
73. Deniz S, Şengül A, Aydemir Y, Çeldir Emre J, Özhan MH. Clinical factors and comorbidities affecting the cost of hospital-treated COPD. *Int J Chron Obstruct Pulmon Dis* 2016;**11**:3023–30. https://doi.org/10.2147/COPD.S120637.
74. Piepoli MF, Hoes AW, Agewall S, Albus C, Brotons C, Catapano AL, et al. 2016 European guidelines on cardiovascular disease prevention in clinical practice: the Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts) developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). *Eur Heart J* 2016;**37**(29):2315–81. https://doi.org/10.1093/eurheartj/ehw106.

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Original Research

The impact of a complex school nutrition intervention on double burden of malnutrition among Thai primary school children: a 2-year quasi-experiment

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ABSTRACT

Objective: This study assessed the impacts of the *Dekthai Kamsai* programme on overweight/obesity, underweight and stunting among male and female primary school students.
Study design: A quasi-experiment was conducted in 16 intervention and 19 control schools across Thailand in 2018 and 2019. In total, 896 treated and 1779 control students from grades 1 to 3 were recruited. In intervention schools, a set of multifaceted intervention components were added into school routine practices. Anthropometric outcomes were measured at baseline and at the beginning and end of every school term.
Methods: Propensity score matching with linear and Poisson difference-in-difference analyses were used to adjust for the non-randomisation and to analyse the intervention's effects over time.
Results: Compared with controls, the increases in mean BMI-for-age Z-score (BAZ) and the incidence rate of overweight/obesity were lower in the intervention schools at the 3rd, 4th and 8th measurements and the 3rd measurement, respectively. The decrease in mean height-for-age Z-score (HAZ) was lower at the 4th measurement. The decrease in the incidence rate of wasting was lower at the 5th, 7th and 8th measurements. The favourable impacts on BAZ and HAZ were found in both sexes, while the favourable impact on overweight/obesity and unfavourable impact on wasting were found in girls.
Conclusions: This intervention might be effective in reducing BAZ, overweight/obesity, poor height gain, but not wasting. These findings highlight the benefits of a multifaceted school nutrition intervention and a need to incorporate tailor-made interventions for wasting to comprehensively address the double burden of malnutrition.

Introduction

The double burden of malnutrition in children, which is defined as the coexistence of over- and under-nutrition, is a leading cause of global disability-adjusted life years (DALYs).[1] This threat undermines the global capacity to achieve the United Nations' Sustainable Development Goals (SDGs) not only because nutrition is a

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part of SDG2 (End hunger, achieve food security and improved nutrition and promote sustainable agriculture) but also nutrition contributes to ensuring healthy lives and human well-being (SDG3) and development.[2,3]

Malnutrition is extremely challenging to address due to its complex aetiology.[3] Current progress in addressing it is slow and unlikely to achieve the global nutrition targets for 2025.[4] Children aged 5–19 years are often neglected, as they are not prioritised in global targets. In this age group, there has been a rapid increase in overnutrition (overweight and obesity) as well as the continued presence of undernutrition (wasting and stunting) in low- and middle-income countries.[4,5] There is evidence that school nutrition interventions have the potential to decrease overweight and obesity in school-aged children and adolescents; however, most studies were carried out in high-income countries and China.[6,7] Moreover, the effects of interventions on undernutrition among school-aged children are rarely reported, and there is limited information on whether boys and girls respond differently to school-based interventions. Therefore, more evidence, especially from diverse low- and middle-income countries, is needed to guide the effective implementation of school-based nutrition interventions to address the double burden of malnutrition.

The double burden of malnutrition among school-aged children is increasing in Thailand because of a rise in child obesity (5.8%–18.1% between 1995 and 2014) alongside with a persistence of undernutrition (14.4% wasting, 2.9% stunting in 2014).[8] Although a free school lunch scheme has been implemented in public primary schools in Thailand since 1999,[9] the double burden of malnutrition among Thai school-aged children still continues to rise. This indicates that providing free school lunch alone is insufficient.

Therefore, a school nutrition intervention called the '*Dekthai Kamsai* Programme' was implemented in primary schools to address malnutrition in school-aged children. It is a multipurpose, multicomponent and multiactor school nutrition intervention based on lessons learned from previous school nutrition programmes in Thailand.[10] A recent study, published in February 2023, indicated that this programme might reduce overweight and obesity among school-aged children.[11] However, since the study was cross-sectional with no baseline data and it did not assess the impact of the programme on undernutrition, further research should be conducted to examine whether the programme really had impacts on the double burden of malnutrition among the children and in both sexes. From 2018 to 2019, a 2-year quasi-experiment assessing the impacts of *Dekthai Kamsai* Programme was conducted. Our study analysed the data obtained from this quasi-experiment to assess the impacts of the *Dekthai Kamsai* programme on overweight/obesity, wasting and stunting among different sexes of primary school students.

Methods

Study design and participants

This study analysed data from a 2-year quasi-experiment conducted in 2018 and 2019. A convenience sample of 50 public primary schools were invited to participate in the study. Thirty-five schools accepted the invitation, consisting of 16 intervention schools and 19 control schools from 12 provinces. The intervention schools were schools located in major provinces across different regions in Thailand and willing to implement the programme. Control schools were schools located in the same provinces as the intervention schools and willing to participate as controls in this study. All students from grades 1 to 3 in these schools were eligible for inclusion. In total, 2675 students, consisting of 896 students from intervention schools and 1779 students from control schools, were recruited into this study. This sample size had 97% power to detect a difference in the rates of overweight and obesity of 20% in intervention and 30% in control groups, respectively, using a two-tailed significance level of 0.05 and adjusted for clustering.[12] These overweight and obesity rates were estimated based on the prevalence of overweight among Thai school-aged children in 2014[8] and a pooled effect of school-based obesity tackling programmes implemented globally in 2014.[13] Written informed consent was obtained from both students and their parents/caretakers with assistance from school staff. Ethical approvals were granted by the Institute for the Development of Human Research Protections (IHRP 021-2563) and London School of Hygiene and Tropical Medicine (LSHTM Ref. No.26555). The process of recruitment is shown in Fig. 1.

Intervention design

The *Dekthai Kamsai* programme was developed by a multidisciplinary working group using lessons learned and tools available from previous school initiatives.[10] The programme was intended to build the capacity of primary schools to improve nutrition and child development among children in their schools, while avoiding unacceptable school staff workloads to gain acceptance and ensure sustainability. The programme's components were designed with an aim to integrate nutrition promotion into regular practices of primary schools rather than introducing additional duties. This programme was implemented on an annual basis according to the programme's and schools' annual budgets and action plans.

The programme strengthened the schools' capacity to implement eight synergistic components, as detailed in Table S1. Broadly, they were related to 1) healthy food provision; 2) school farm and garden; 3) health and nutritional status monitoring; 4) school co-operatives and vocational training; 5) personal health and hygiene promotion; 6) school sanitation; 7) basic health service; and 8) agriculture, nutrition and health education. The intervention schools were required to be competent in implementing the 'healthy food provision' and 'health and nutritional status monitoring' components. Other components were complementary components. The implementation strategies of these components were adaptable to suit the schools' contexts, for example, schools are allowed to provide local food menus with equivalent nutritional values to standard school meals and choose traditional dances or active plays over common sports to promote students' physical activity. Each intervention school formed a working group to integrate these components into the school's routine practices and communicate with class teachers who engaged the students in the programme implementation. Training courses, materials and onsite

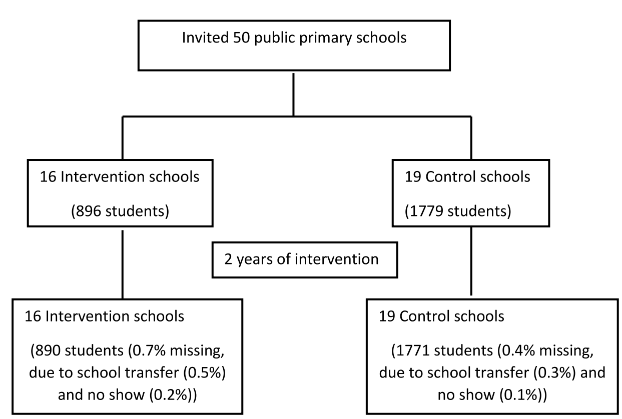

Fig. 1. Participant recruitment and retention.

visits were provided to support the teachers, students and parents. The comparison between the *Dekthai Kamsai* implementation and control schools' routine practices is described in Table S1.

The programme also created a platform for schools to obtain support from authorities at the local level by having five organisations, including the Ministry of Education, Ministry of Public Health, Ministry of Interior, Ministry of Agriculture and Cooperatives, and the National Electronics and Computer Technology Centre, sign a memorandum of understanding to provide support for the schools to implement these components. The programme encouraged schools to work together with communities to ensure a sufficient supply of safe and fresh food ingredients. *Dekthai Kamsai* annual conferences were organised for the intervention schools to share their knowledge and experiences. Intervention schools with excellent practices were promoted as role models, and their experiences were shared on social media and television programmes for facilitating mutual learning. Control schools continued to operate their routine practices.

Outcome measurement and data collection

Anthropometric measurements were conducted by class teachers who were trained by local health personnel. This training is routinely done in all Thai primary schools and did not differ between the intervention and control schools. Students' weights and heights were measured using the schools' calibrated digital scales to the nearest 0.1 kg and portable stadiometers to the nearest 0.1 cm. Consistent measuring instruments and methods were used to measure the children within each school throughout the study period. Data collection was conducted at the beginning and end of each school term, with a total of eight data collection points in the years 2018 and 2019. The first and eighth measurements were conducted at the beginning and end of the programme. The long school break (i.e. 6 weeks) occurred between the 4th and 5th measurements.

Reliability of staff's measurements was assessed by researchers using a method previously described.[14] The weights and heights of 364 students from eight randomly selected schools (i.e. 4 intervention and 4 control schools) were measured independently by school staff using their regular measuring instruments and the research team using a digital scale (Tanita, HD382, Tokyo, Japan) to the nearest 0.1 kg and a portable stadiometer (Institute of Nutrition, Mahidol University, Thailand) to the nearest 0.1 cm. The results showed excellent agreement between the school staff's and research team's measurements (the intraclass correlations coefficient (ICC) were: weight ICC = 0.99, height ICC = 0.99, body mass index (BMI) ICC = 0.99 and BMI *z* score ICC = 0.99).

Statistical analysis

Outcome variables included BMI (kg/m^2), BMI-for-age Z-scores (BAZ), height-for-age Z-scores (HAZ), wasting, stunting, and overweight and obesity. The Z-scores were calculated using the World Health Organization growth reference data.[15] Children were categorised as wasted or stunted if their BAZ or HAZ, respectively, were less than -2SD. They were categorised as overweight and obese if their BAZ were more than 1SD and 2SD, respectively.

Although the distributions of continuous outcomes (i.e. BMI, BAZ and HAZ) were non-normal, the large sample size of this study allows the application of parametric statistical methods without having to transform the data.[16] The independent *t*-test was used to compare the mean BMI, BAZ and HAZ of the intervention and control groups at baseline. For binary variables (wasted, overweight or obesity and stunted), the chi-squared test was used to compare the intervention and control groups at baseline. We used nearest neighbour propensity score matching with the code ‘psmatch2’ to adjust for the non-randomised design of this study in STATA version 17.[17,18] Logistic regression was performed to estimate propensity score for each observation using the following baseline characteristics: *urbanicity, sex, age, parental occupation* and *person who usually cooked meals for the student*. Treated participants were matched with seven nearest neighbour controls within 0.2 caliper. To determine the effects of the programme, the difference-in-difference approach with linear and Poisson regression models for panel data was used for continuous outcomes (BMI, BAZ and HAZ) and binary outcomes (overweight/obesity, wasting and stunting), respectively. All models were adjusted for the clustering effects of school because the sampling process and treatment assignment were done at the school level and also students in the same school were exposed to the same context.[19,20] Significance tests were set at $\alpha = 0.05$.

Results

Table 1 describes the sociodemographic and anthropometric characteristics of the control and intervention groups at baseline. There were no statistically significant differences between intervention and control groups in terms of gender, average age, parental occupation, the person who usually cooked meals for the student, mean BMI, mean BAZ and percentage of stunted children. However, there were significant intergroup differences in the percentage of students living in urban areas, the participants mean HAZ and the percentages of overweight/obese and wasted participants. Of 1779 controls, 1609 controls were good matches for 896 treated participants and were included in the analyses. The balancing property was satisfied with Rubins' B less than 25% and R between 0.5 and 2 (Table S2).

Mean BMI and BAZ increased over time in both groups (Table S3). The effect of the intervention on the students' BAZ was shown in Table 2. The increase in mean BAZ in the intervention

Table 1
Sociodemographic and anthropometric characteristics of children in intervention and control schools at baseline.

Variable	Intervention group ($N = 896$)	Control group ($N = 1779$)	*P*-value
Male (%)	50.7	54.1	0.090
Age (years) (mean (SD[d]))	7.7 (1.08)	7.8 (1.05)	0.070
Live in urban area (%)	50.5	73.8	<0.0001[e]
Parental occupation (%)			
Daily wage worker	42.3	41.2	0.432
Farmer	10.7	11.7	
Business owner	11.0	11.6	
Private sector employee	15.5	15.5	
Civil servant	4.5	4.1	
Unemployed	3.5	5.1	
Other, e.g. monk, died or lost contact	12.5	10.8	
Person who usually cooked meals for the student (%)			
Mother	51.5	53.0	0.321
Other family member	14.6	14.4	
Oneself	27.5	24.8	
Other, e.g. food vendors	6.4	7.8	
BMI[a] kg/m^2 (mean (SD[d]))	16.64 (3.76)	16.85 (4.28)	0.222
BAZ[b] (mean (SD[d]))	0.15 (1.65)	0.09 (2.17)	0.473
HAZ[c] (mean (SD[d]))	−0.33 (1.16)	0.05 (1.32)	<0.0001[e]
Overweight and obese (%)	26.1	32.6	0.001[e]
Wasted (%)	5.8	12.5	<0.0001[e]
Stunted (%)	5.6	4.8	0.407

[a] BMI – body mass index.
[b] BAZ – body mass index-for-age *Z*-score.
[c] HAZ – height-for-age *Z*-score.
[d] SD – Standard deviation.
[e] Significant difference at $P < 0.05$.

group was significantly lower than that of the control group at the 3rd, 4th, 6th, 7th and 8th measurements. This favourable trend was found in both boys (at the 3rd, 4th, 6th and 8th measurements) and girls (at the 3rd, 4th, 7th and 8th measurements).

The increase in mean BMI was significantly lower in the intervention compared with the control group at the 3rd (−0.267, 95% CI −0.476, −0.058, $P = 0.014$) and 4th measurements (−0.333, 95% CI −0.602, −0.065, $P = 0.017$) (Table S4). This favourable trend was found in both boys and girls.

Mean HAZ in the intervention group did not change much, whereas mean HAZ in the control group decreased over time (Table S3). Overall, the decrease in mean HAZ in the intervention group was significantly lower than the control group only at the 4th measurement (Table 3). This trend was found in both boys and girls.

The percentage of overweight or obese students increased over time in intervention and control groups (Fig. S1). The increase in incidence rate of being overweight or obese in the intervention group was significantly lower than in the control group at the 3rd measurement (Table 4). This trend was found in girls, but not in boys.

The percentage of wasted students decreased in both groups in 2018 and continued to decrease in only the control group in 2019 (Fig. S2). Compared with the control group, the decrease in incidence rate of being wasted in the intervention group was significantly lower at the 5th, 7th and 8th measurements (Table 5). The decrease in incidence rate of being wasted in treated girls was significantly lower than untreated girls at the 4th, 5th, 7th and 8th measurements. There was no significant difference between treated and untreated boys.

Table 2
Effects of the intervention on body mass index *Z*-scores (BAZ) comparing children in intervention and control schools.

Variable	Coefficient	95% CI	*P*-value
Effect on both sexes (*N* = 2505)			
Reference: 1st measurement			
2018 (Baseline)			
2nd measurement	−0.110	−0.238, 0.019	0.092
3rd measurement	−0.190	−0.326, −0.054	0.007*
4th measurement	−0.219	−0.375, −0.065	0.007*
2019			
5th measurement	−0.171	−0.354, 0.012	0.067
6th measurement	−0.246	−0.463, −0.029	0.028*
7th measurement	−0.239	−0.450, −0.027	0.028*
8th measurement (Endline)	−0.307	−0.524, −0.090	0.007*
Effect on boys (*n* = 1334)			
Reference: 1st measurement			
2018 (Baseline)			
2nd measurement	−0.118	−0.247, 0.011	0.072
3rd measurement	−0.209	−0.360, −0.059	0.008*
4th measurement	−0.223	−0.392, −0.054	0.011*
2019			
5th measurement	−0.180	−0.383, 0.023	0.081
6th measurement	−0.272	−0.503, −0.040	0.023*
7th measurement	−0.228	−0.461, 0.006	0.056
8th measurement (Endline)	−0.291	−0.521, −0.060	0.015*
Effect on girls (*n* = 1171)			
Reference: 1st measurement			
2018 (Baseline)			
2nd measurement	−0.101	−0.246, 0.044	0.165
3rd measurement	−0.171	−0.315, −0.028	0.020*
4th measurement	−0.217	−0.372, −0.061	0.008*
2019			
5th measurement	−0.162	−0.349, 0.025	0.087
6th measurement	−0.219	−0.440, 0.002	0.052
7th measurement	−0.250	−0.460, −0.040	0.021*
8th measurement (Endline)	−0.325	−0.547, −0.102	0.005*

Used linear regression difference-in-difference, * Significant increase at $P < 0.05$.

Table 3
Effects of the intervention on height-for-age *Z*-scores (HAZ) comparing children in intervention and control schools.

Variable	Coefficient	95% CI	*P*-value
Effect on both sexes (*N* = 2505)			
Reference: 1st measurement			
2018 (Baseline)			
2nd measurement	0.011	−0.066, 0.087	0.778
3rd measurement	0.071	−0.004, 0.147	0.064
4th measurement	0.141	0.010, 0.271	0.036*
2019			
5th measurement	0.082	−0.063, 0.226	0.258
6th measurement	0.113	−0.065, 0.292	0.206
7th measurement	0.175	−0.016, 0.366	0.072
8th measurement (Endline)	0.207	−0.033, 0.446	0.089
Effect on boys (*n* = 1334)			
Reference: 1st measurement			
2018 (Baseline)			
2nd measurement	0.009	−0.650, 0.084	0.802
3rd measurement	0.070	−0.0070.146	0.073
4th measurement	0.135	0.009, 0.261	0.037*
2019			
5th measurement	0.063	−0.076, 0.202	0.361
6th measurement	0.094	−0.067, 0.254	0.243
7th measurement	0.155	−0.013, 0.323	0.070
8th measurement (Endline)	0.167	−0.041, 0.375	0.112
Effect on girls (*n* = 1171)			
Reference: 1st measurement			
2018 (Baseline)			
2nd measurement	0.012	−0.070, 0.094	0.767
3rd measurement	0.073	−0.008, 0.154	0.076
4th measurement	0.146	0.006, 0.286	0.042*
2019			
5th measurement	0.100	−0.059, 0.258	0.210
6th measurement	0.133	−0.073, 0.338	0.197
7th measurement	0.194	−0.029, 0.417	0.086
8th measurement (Endline)	0.194	−0.029, 0.417	0.086

Used linear regression difference-in-difference, * Significant increase at $P < 0.05$.

There was no significant difference comparing the changes in incidence rate of being stunted between the intervention and control groups and between boys and girls.

Discussion

The results from this study indicate that the *Dekthai Kamsai* Programme had favourable impacts on BMI, BAZ, HAZ in both sexes and overweight/obesity in girls after one school term. However, these favourable changes were interrupted by the long school break between the two school years. In terms of wasting, the programme had no positive impact among boys and may had a negative impact among girls. This programme might be effective in reducing the risks of becoming overweight or obese and stunted; however, there was a room for improvement, especially in addressing wasting.

These results for overnutrition are consistent with a recent cross-sectional analysis of the *Dekthai Kamsai* Programme,[11] which indicated that the programme reduced the overweight and obesity rates among children in the intervention compared with control schools.

The effect size of the *Dekthai Kamsai* programme on students' BAZ was greater than the pooled effect of 12 multicomponent school nutrition programmes implemented in Asia during the past decade (−0.190, −0.220, −0.246, −0.239 and −0.307 vs. −0.07).[7] Among these previous 12 school nutrition programmes, six interventions significantly reduced students' BAZ with effect sizes ranging from −0.03 to −0.14.[21–26] Similar to the *Dekthai Kamsai* programme, the previous interventions were multicomponent interventions; however, they differed in terms of the number of

Table 4
Effects of the intervention on the incidence rate of overweight comparing children in intervention and control schools in 2018 and 2019[b].

Variable	IRR[a]	95% CI	*P*-value
Effect on both sexes (*N* = 2505)			
Reference: 1st measurement			
2018 (Baseline)			
2nd measurement	0.953	0.879, 1.034	0.249
3rd measurement	0.903	0.819, 0.995	0.039*
4th measurement	0.903	0.805, 1.013	0.082
2019			
5th measurement	0.987	0.807, 1.207	0.900
6th measurement	0.932	0.794, 1.093	0.384
7th measurement	0.963	0.803, 1.154	0.681
8th measurement (Endline)	0.969	0.805, 1.167	0.742
Effect on boys (*n* = 1334)			
Reference: 1st measurement			
2018 (Baseline)			
2nd measurement	0.955	0.869, 1.049	0.337
3rd measurement	0.932	0.831, 1.046	0.235
4th measurement	0.945	0.833, 1.071	0.377
2019			
5th measurement	1.011	0.802, 1.274	0.927
6th measurement	0.937	0.783, 1.122	0.481
7th measurement	0.983	0.775, 1.247	0.890
8th measurement (Endline)	1.005	0.806, 1.254	0.961
Effect on girls (*n* = 1171)			
Reference: 1st measurement			
2018 (Baseline)			
2nd measurement	0.953	0.839,1.082	0.460
3rd measurement	0.869	0.762,0.991	0.037*
4th measurement	0.858	0.727, 1.012	0.069
2019			
5th measurement	0.958	0.764,1.201	0.709
6th measurement	0.925	0.772, 1.109	0.399
7th measurement	0.938	0.762, 1.153	0.542
8th measurement (Endline)	0.922	0.743, 1.145	0.464

[a] IRR – incidence rate ratio.
[b] Used random effects Poisson regression difference-in-difference analyse, * Significant increase at $P < 0.05$.

Table 5
Effects of the intervention on the incidence rate of wasting comparing children in intervention and control schools in 2018 and 2019[b].

Variable	IRR[a]	95% CI	*P*-value
Effect on both sexes (*N* = 2505)			
Reference: 1st measurement			
2018 (Baseline)			
2nd measurement	1.087	0.749, 1.577	0.662
3rd measurement	1.178	0.743, 1.867	0.487
4th measurement	1.199	0.783, 1.836	0.403
2019			
5th measurement	1.671	1.041, 2.682	0.033*
6th measurement	1.611	0.972, 2.669	0.064
7th measurement	1.771	1.082, 2.899	0.023*
8th measurement (Endline)	2.229	1.116, 4.453	0.023*
Effect on boys (*n* = 1334)			
Reference: 1st measurement			
2018 (Baseline)			
2nd measurement	1.114	0.709, 1.750	0.640
3rd measurement	1.213	0.681, 2.162	0.513
4th measurement	0.824	0.451, 1.503	0.527
2019			
5th measurement	1.230	0.734, 2.061	0.431
6th measurement	1.419	0.834, 2.412	0.197
7th measurement	1.713	0.918, 3.198	0.091
8th measurement (Endline)	1.671	0.769, 3.634	0.195
Effect on girls (*n* = 1171)			
Reference: 1st measurement			
2018 (Baseline)			
2nd measurement	1.040	0.620, 1.747	0.881
3rd measurement	1.147	0.752, 1.750	0.525
4th measurement	1.748	1.081, 2.826	0.027*
2019			
5th measurement	2.334	1.342, 4.058	0.003*
6th measurement	1.857	0.977, 3.530	0.059
7th measurement	1.822	1.033, 3.213	0.038*
8th measurement (Endline)	3.031	1.411, 6.511	0.004*

[a] IRR – incidence rate ratio.
[b] Used random effects Poisson regression difference-in-difference analyse, * Significant increase at $P < 0.05$.

components and intervention intensity. In general, the previous interventions focused on either physical activity and nutrition education or healthy food provision and nutrition education, whereas the more comprehensive *Dekthai Kamsai* programme aimed at improving physical activity, the provision of healthy school lunches, nutrition education, school sanitation and the school's capacity for monitoring and addressing malnutrition. Likewise, the level of physical activity implemented in the *Dekthai Kamsai* programme (i.e. 30-min per day of moderate to vigorous activity) was more intense than that implemented in five other programmes.[21,23–26] There was only one other programme with a more intense physical activity component (i.e. 60-min of daily vigorous activity).[22] Comprehensiveness and intensity of interventions may partially explain the different effect sizes of school nutrition interventions in Asia. Further research is needed to confirm the relationships between the comprehensiveness and intensity of interventions and effect sizes of school nutrition interventions in the Asian context.

The *Dekthai Kamsai* programme consisted of components that had been identified as key components for school-based obesity tackling by previous studies. Meta-analyses of school nutrition interventions confirm that physical activity, even as a single component, reduced children's BMI or BAZ, and that school gardening increased fruit and vegetable consumption among school-aged children.[6,7,27,28] School gardening and fun physical activities also increased the time spent in physical activity of moderate-to-vigorous intensity among school-aged children.[29–31] Two meta-analyses found that integrating agriculture, nutrition and health education into curricula increases the effectiveness of school-based nutrition interventions.[6,31] Real-time outcome monitoring was a key success factor of a successful adaptive community-based nutrition intervention[32] and a well-functioning feedback loop plays an important role in improving school-based nutrition interventions.[33] For diet interventions, the results are inconsistent, which might reflect the wide range of services in different school-based interventions.[7] Not all previous interventions provided school meals that met nutritional standards,[7] whereas those following dietary guidelines and school meal standards were effective.[34] The school lunches provided in the *Dekthai Kamsai* programme met one-third of the recommended nutrient reference values of children. Nevertheless, our findings suggested that one healthy school meal was not sufficient to address wasting in the intervention schools. Although our study adds to the current body of evidence that a combination of the *Dekthai Kamsai* components improved children's BMI, BAZ and HAZ and reduced the incidence rate of overweight and obesity, the contribution of individual components is unknown.

Interesting patterns were observed in anthropometric changes between the intervention and control groups. Firstly, the gap between the groups increased with time of exposure in each school year and decreased slightly during the 6-week school break between school years. This trend suggests that direct intervention exposure is important to maintain the intervention's effects. This finding is consistent with the finding from a recent cross-sectional study[11] that the impact on overnutrition of the *Dekthai Kamsai* programme was not sustainable in dropped-out schools. Secondly, the differences were statistically significant after the first school term for BAZ (at the 3rd, 4th, 6th, 7th and 8th measurements) and HAZ (at the 4th measurement). This finding shows that this complex school nutrition intervention, in a semi-urban and mixed socio-economic status context, needs more than one school term to show significant changes. This finding highlights the importance of providing sufficient time for intervention exposure. At present, there is no evidence regarding the duration required to improve anthropometric outcomes in school nutrition programmes,[6,7,27] which is crucial for intervention programme planning and evaluation design. Our analyses and the previous analyses of the *Dekthai Kamsai* programme[11] indicate long-term continuity is important.

Our findings also highlight the importance of monitoring the anthropometric status of school children multiple times over the school year. Our study captured the pattern of changes over the school terms and school breaks, which encouraged the identification of the intervention gaps. Such data provides important insights to inform policy decisions on what works, for whom, and under what circumstances, which is required to inform policy decisions.[35,36]

Strengths and limitations

The strength of this study is that it provides evidence related to the double burden of malnutrition rather than obesity alone. Such evidence is scarce and yet it is important to obtain because in many parts of the world, school children suffer from both over- and/or under-nutrition.[4,5] School nutrition interventions and evaluations in Asia focused primarily on childhood obesity,[7] but not on wasting and stunting, which are also important problems in Asia.[3] In addition, it provides evidence regarding the impacts of school nutrition interventions implemented in Southeast Asia where relevant literature is very limited.

This study, however, has some limitations. Firstly, the collaborative nature of the *Dekthai Kamsai* programme and the ethical and equity considerations prevented a randomised control trial, which meant causal probability inferences could not be drawn given biases inherent to a quasi-experimental design. We partially adjusted for this limitation by using a propensity score matching method in conjunction with a difference-in-difference approach. These complementary statistical methods were initiated to reduce bias due to the non-randomised design of public policy impact assessments.[20] Secondly, the measurements of body weight and height were done using the school's measuring instruments by school staff who were not blinded to outcomes, which raises questions about the reliability of the data and the introduction of bias. However, the results of our reliability study and the data pattern continuity indicate that the quality of the data obtained from the schools was adequate. Thirdly, the *Dekthai Kamsai* programme was implemented with a realist approach, which meant it was implemented solely by local multisectoral actors and was adaptable to local capacities and needs. By this nature, it could lead to implementation variations among schools in the programme and reduce intervention fidelity. The evaluation design and nature of the programme limits our ability to assess the causal relationships between the individual components in the intervention and outcomes. However, this approach enhanced stakeholders' buy-in and context appropriateness.

Conclusion

This study adds to the current body of evidence that a school-based nutrition intervention with multifaceted components might be effective in reducing the incidence of overnutrition and increasing HAZ among Thai primary school-aged children after one school term. However, it was not effective in reducing wasting, especially among girls. This study stresses the need to provide a separate set of services within the programme, for wasted children, to strengthen its impact on the double burden of malnutrition. It also shows the feasibility of implementing an effective multiple-component school-based intervention within the routine practices of Thai public primary schools with sufficient financial and technical support to initiate and sustain the intervention.

Author statements

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Ethical approval

Ethical approval was granted by the Institute for the Development of Human Research Protections (IHRP 021-2563) and London School of Hygiene and Tropical Medicine (LSHTM Ref. No.26555).

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Competing interests

The authors declare that they have no conflict of interest.

Contributors

SP contributed to conceptualization, methodology, formal analysis, data curation and writing – original draft preparation; LL, EF, CD, VT, JB, SL and CW contributed to supervision, review and editing.

Patient and public involvement

Governmental agencies, non-governmental agencies and an inter-disciplinary working group responsible for school-based health policy were involved in the design, implementation and report of findings of this intervention. The staff of participating schools took part in designing strategies used in some components of the intervention.

Consent for publication

Not applicable.

Availability of data and materials

The data sets used during the current study are available from the corresponding author on reasonable request.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.puhe.2023.08.023.

References

1. Murray CJL, Aravkin AY, Zheng P, Abbafati C, Abbas KM, Abbasi-Kangevari M, et al. Global burden of 87 risk factors in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet* 2020;**396**(10258):1223–49.
2. The United Nations. *General Assembly resolution 66/288, the future we want, A/RES/66/288 (27 July 2012)*. 2012. https://www.un.org/en/development/desa/population/migration/generalassembly/docs/globalcompact/A_RES_66_288.pdf. [Accessed 6 May 2023].
3. Development Initiatives. *Global nutrition report 2017: nourishing the SDGs*. 2017. Bristol, UK.
4. Development Initiatives. *Global nutrition report 2021: the state of global nutrition*. 2021. Bristol, UK.
5. Development Initiatives. *Global nutrition report 2020: action on equity to end malnutrition*. 2020. Bristol, UK.
6. Liu Z, Xu HM, Wen LM, Peng YZ, Lin LZ, Zhou S, et al. A systematic review and meta-analysis of the overall effects of school-based obesity prevention interventions and effect differences by intervention components. *Int J Behav Nutr Phys Act* 2019;**16**(1):95. https://doi.org/10.1186/s12966-019-0848-8. PMID: 31665040; PMCID: PMC6819386.
7. Pongutta S, Ajetunmobi O, Davey C, Ferguson E, Lin L. Impacts of school nutrition interventions on the nutritional status of school-aged children in Asia: a systematic review and meta-analysis. *Nutrients* 2022;**14**:589. https://doi.org/10.3390/nu14030589.
8. Akeplakorn W. *The Fifth Thailand health examination survey (children's health) 2014*. Nonthaburi: HSRI; 2016.
9. School Lunch Project-Fund Bureau. *History of the school lunch fund*. 2017. http://www.obecschoollunch.com/history/. [Accessed 2 December 2020].
10. FSNHPI. *Dekthai Kamsai schools*. 2023. https://www.dekthaikamsai.com/paper/363. [Accessed 6 May 2023].
11. Kanchanachitra M, Angeles G. Impact of a school-based nutrition intervention in preventing overweight and obesity in children in Thailand. *J Sch Health* 2023;**93**(2):140–7. https://doi.org/10.1111/josh.13253. Epub 2022 Oct 11. PMID: 36217922; PMCID: PMC10092697.
12. Batistatou E, Roberts C, Roberts S. Sample size and power calculations for trials and quasi-experimental studies with clustering. *Stata J* 2014;**14**(1):159–75. https://doi.org/10.1177/1536867X1401400111.
13. Mahmood S, Perveen T, Dino A, Ibrahim F, Mehraj J. Effectiveness of school-based intervention programs in reducing prevalence of overweight. *Indian J Community Med* 2014;**39**(2):87–93. https://doi.org/10.4103/0970-0218.132724. PMID: 24963224; PMCID: PMC4067935.
14. Berkson SS, Espinola J, Corso KA, Cabral H, McGowan R, Chomitz VR. Reliability of height and weight measurements collected by physical education teachers for a school-based body mass index surveillance and screening system. *J Sch Health* 2013;**83**(1):21–7. https://doi.org/10.1111/j.1746-1561.2012.00743.x. PMID: 23253287.
15. de Onis M, Onyango AW, Borghi E, Siyam A, Nishida C, Siekmann J. Development of a WHO growth reference for school-aged children and adolescents. *Bull World Health Organ* 2007;**85**(9):660–7. https://doi.org/10.2471/blt.07.043497. PMID: 18026621; PMCID: PMC2636412.
16. Kwak SG, Kim JH. Central limit theorem: the cornerstone of modern statistics. *Korean J Anesthesiol* 2017 Apr;**70**(2):144–56. https://doi.org/10.4097/kjae.2017.70.2.144. Epub 2017 Feb 21. PMID: 28367284; PMCID: PMC5370305.
17. Heinrich C, Maffioli A, Valdivia G. *A primer for applying ropensity score matching: impact-evaluation guideline*. Washington, DC: Inter-American Development Bank; 2010.
18. Leuven E, Sianesi B. PSMATCH2: stata module to perform full Mahalanobis and propensity score matching, common support graphing, and covariate imbalance testing. *Stat Softw Comp* 2018. S432001, Boston College Department of Economics.
19. Fredriksson A, Oliveira GM de. Impact evaluation using difference-in-differences. *RAUSP Manag J* 2019;**54**(4):519–32.
20. Stuart EA, Huskamp HA, Duckworth K, Simmons J, Song Z, Chernew M, et al. Using propensity scores in difference-in-differences models to estimate the effects of a policy change. *Health Serv Outcomes Res Methodol* 2014;**14**(4):166–82. https://doi.org/10.1007/s10742-014-0123-z. PMID: 25530705; PMCID: PMC4267761.
21. Meng L, Xu H, Liu A, van Raaij J, Bemelmans W, Hu X, et al. The costs and cost-effectiveness of a school-based comprehensive intervention study on childhood obesity in China. *PLoS One* 2013;**8**(10):e77971. https://doi.org/10.1371/journal.pone.0077971. PMID: 24205050; PMCID: PMC3800134.
22. Guo H, Zeng X, Zhuang Q, Zheng Y, Chen S. Intervention of childhood and adolescents obesity in Shantou city. *Obes Res Clin Pract* 2015;**9**(4):357–64. https://doi.org/10.1016/j.orcp.2014.11.006. Epub 2015 Jan 13. PMID: 25596004.
23. Amini M, Djazayery A, Majdzadeh R, Taghdisi MH, Sadrzadeh-Yeganeh H, Abdollahi Z, et al. A school-based intervention to reduce excess weight in overweight and obese primary school students. *Biol Res Nurs* 2016;**18**(5):531–40. https://pubmed.ncbi.nlm.nih.gov/27358261/.
24. Xu H, Li YY, Zhang Q, Hu X, Liu A, Du S, et al. Comprehensive school-based intervention to control overweight and obesity in China: a cluster randomized controlled trial. *Asia Pac J Clin Nutr* 2017;**26**(6):1139–51. https://pubmed.ncbi.nlm.nih.gov/28917242/.
25. Koo HC, Poh BK, Abd Talib R. The GReat-child™ trial: a quasi-experimental intervention on whole grains with healthy balanced diet to manage childhood obesity in Kuala Lumpur, Malaysia. *Nutrients* 2018;**10**(2):156. https://doi.org/10.3390/nu10020156. PMID: 29385769; PMCID: PMC5852732.
26. Habib-Mourad C, Ghandour LA, Maliha C, Dagher M, Kharroubi S, Hwalla N. Impact of a three-year obesity prevention study on healthy behaviors and BMI among Lebanese schoolchildren: findings from Ajyal Salima program. *Nutrients* 2020;**12**(9):2687. https://doi.org/10.3390/nu12092687. PMID: 32899135; PMCID: PMC7551295.
27. Feng L, Wei DM, Lin ST, Maddison R, Ni Mhurchu C, Jiang Y, et al. Systematic review and meta-analysis of school-based obesity interventions in mainland China. *PLoS One* 2017;**12**(9):e0184704. https://doi.org/10.1371/journal.pone.0184704. PMID: 28910362; PMCID: PMC5598996.
28. Qi Y, Hamzah SH, Gu E, Wang H, Xi Y, Sun M, et al. Is school gardening combined with physical activity intervention effective for improving childhood obesity? A systematic review and meta-analysis. *Nutrients* 2021;**13**(8). https://doi.org/10.3390/nu13082605. PMID: 34444765; PMCID: PMC8402215.
29. Wells NM, Myers BM, Henderson Jr CR. School gardens and physical activity: a randomized controlled trial of low-income elementary schools. *Prev Med* 2014;**69**(Suppl. 1):S27–33. https://doi.org/10.1016/j.ypmed.2014.10.012. Epub 2014 Oct 16. PMID: 25456803.
30. Chang YY, Su WC, Tang IC, Chang CY. Exploring the benefits of school gardening for children in Taiwan and identifying the factors influencing these benefits. *HortTechnol Hortte* 2016;**26**(6):783–92. https://doi.org/10.21273/HORTTECH03074-16.
31. Ohly H, Gentry S, Wigglesworth R, Bethel A, Lovell R, Garside R. A systematic review of the health and well-being impacts of school gardening: synthesis of quantitative and qualitative evidence. *BMC Publ Health* 2016 Mar 25;**16**:286. https://doi.org/10.1186/s12889-016-2941-0. Erratum in: BMC Public Health. 2016 Oct 5;16(1):1051. PMID: 27015672; PMCID: PMC4807565.
32. Ruel-Bergeron JC, Hurley KM, Kang Y, Aburto N, Farhikhtah A, Dinucci A, et al. Monitoring and evaluation design of Malawi's right foods at the right time nutrition program. *Eval Program Plann* 2019;**73**:1–9. https://pubmed.ncbi.nlm.nih.gov/30453182/.
33. Schultz L, Ruel-Bergeron J. Considerations for monitoring school health and nutrition programs. *Front Public Health* 2021;**9**:645711. https://doi.org/10.3389/fpubh.2021.645711. PMID: 34336757; PMCID: PMC8322578.
34. Pineda E, Bascunan J, Sassi F. Improving the school food environment for the prevention of childhood obesity: what works and what doesn't. *Obes Rev* 2021;**22**(2):e13176. https://onlinelibrary.wiley.com/doi/full/10.1111/obr.13176.
35. Pawson R, Tilly N. *Realistic evaluation*. London: SAGE Publications; 1997.
36. Langlois ÉV, Daniels KAE, editors. *Evidence synthesis for health policy and systems: a method guide*. Geneva: WHO; 2018.

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Original Research

The interplay between the impact of household's and children's education on the risk of type 2 diabetes and death among older adults: a Danish register-based cohort study

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A B S T R A C T

Objectives: This study aims to assess the association of household's and children's education on the risk of type 2 diabetes (T2D) and subsequent death.
Study design: Danish register-based cohort study.
Methods: In total, 1,021,557 adults were included at their 65th birthday between 2000 and 2018. A multistate survival model was performed to estimate the association of household's and children's education on the transition between the three states: 1) 65th birthday; 2) diagnosis of T2D; and 3) all-cause death.
Results: The incidence rates per 1000 person-years were 9.1 for T2D, 18.4 for death without T2D, and 45.0 for death with T2D. Compared to long household's education and children's education, long household's education combined with either short-medium children's education or no children were associated with a 1.49- (95% confidence interval [CI]: 1.44; 1.54] and 1.69-times (95% CI: 1.61;1.78) higher hazard of T2D, respectively. Short-medium household's education combined with either long children's education or no children were associated with 0.64- (95% CI: 0.62; 0.66) and 0.77-times (95% CI: 0.74; 0.79) lower hazard of T2D, respectively. Compared to long household's education and children's education, any other combination of household's and children's education was associated with higher hazards of death both without and with T2D.
Conclusion: Older adults living in households with long education with no children or children with short-medium education had higher hazards of T2D. Households with short-medium education and no children or children with long education were associated with lower hazards of T2D. Both household's and children's education were associated with higher hazard of death without and with T2D.

Introduction

Type 2 diabetes (T2D) mellitus is a major and fast-growing health problem worldwide[1] with socioeconomic inequality both in the risk of developing the disease[2,3] and the consequences, such as diabetes-related complications and shorter survival.[4–6] This has been identified for the socioeconomic position at the individual and household level.[2–6] Lack of social support has also been associated with both higher risk of T2D and diabetes-related complications.[7] In addition, social support has been found to have a beneficial impact on diabetes self-management.[7]

Recently, there has been a growing interest in the impact of adult children's socioeconomic resources on their parents' health and mortality,[8–19] also referred to as social foreground. Based on Berkman and Glass' theory on how social relations impact health,[20] Torssander has presented three possible mechanisms behind social foreground: 1) social support, 2) social influence, and 3) access to resources.[13] In more detail, the hypothesis is that children with longer education have the resources and knowledge to support and

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influence their parents' health-related behaviour more positively or guide them in the healthcare system resulting in better health and longer lives than children with shorter education. Thus, older adults with children with longer education may be supported by their children to lead a healthier lifestyle reducing their risk of T2D. The children can also support their parents in relation to adherence to treatment if they are diagnosed with T2D. Another theory by Diderichsen on differential vulnerability describes that even when a risk factor is evenly distributed across social groups, its impact on health and death differs due to other underlying risk factors.[21] Hence, it is possible that older adults with fewer socioeconomic resources in their household may be especially vulnerable to disease and death if their adult children also have fewer socioeconomic resources.

To our knowledge, no previous study has assessed either the impact of children's education on older adults' risk of T2D and subsequent death or the possible interplay with household's and children's education. Such knowledge would improve our understanding of possible mechanisms behind social inequality in the incidence and prognostic outcomes of T2D. This study aims to examine the interplay between household's and adult children's socioeconomic resources, measured by educational level, on the risk of T2D, death without and with T2D among older adults. The findings will elucidate whether health professionals should prioritise more resources towards older adults without children or children with shorter education when providing early preventive measures of T2D. Likewise, the findings may also suggest a need for more focus and guidance in the treatment of older adults with T2D and those without children or children with shorter education.

Methods

Study population

The source population in this cohort study consisted of all individuals ($N = 1{,}069{,}477$) born between 1935 and 1953 who lived in Denmark on their 65th birthday (Fig. 1) without a prior diagnosis of T2D or use of antidiabetic medication ($n = 123{,}392$). Individuals with children aged <30 years were excluded to ensure that the children were old enough to have finished their education and influence their parents' health. Fig. 1 shows the selection of the final study population, which consisted of 1,021,557 older adults.

Denmark is a welfare state with universal health care entailing that healthcare services is free of charge; however, there are out of pocket payment on psychologists and medication, yet prescription medication is subsidised partially. Furthermore, there are no tuition fees for most education programs.

Data source

In Denmark, all individuals are given a personal identification number (CPR) at birth or at immigration, and parents and their children can be linked on an individual level through the CPR-number in the Danish Civil Registration System.[22] Using CPR-linkage, data were retrieved from the Danish National Patient Registry, the Danish National Prescription Registry, and the Population Education Register.[22] The data are anonymised by Statistics Denmark. Thus, ethical approval is not needed for analyses of register-based data in Denmark.

Highest educational attainment of household and children

We identified the number of children (including biological and adopted children) one year before the older adults' 65th birthday (baseline) through CPR-linkage.[22] For children aged ≥30 years, we obtained information on their highest attainted education from the Population Education Register one year prior to their parent's (the older adult) 65th birthday.[22] For the older adults with more than one child, we used the educational information of the child with the highest level of attained education based on the 'dominance' approach.[23] Highest attained household's (the older adult and potential partner) and children's education was categorised as short-medium education (primary school, secondary school, skilled training, higher diplomas, and no education registered in Denmark) and long education (higher education – e.g. bachelor's degree). For older adults living alone, the household's education expressed the person's own education. This information was included in a combined variable of household's and children's educational level with the following categories: 1) long household's education and children's education (reference group) (from now: long/long), 2) long household's education and short-medium children's education (long/short-medium), 3) long household's education and no children (long/no children), 4) short-medium household's education and long children's education (short-medium/long), 5) short-medium household's and children's education (short-medium/short-medium), and 6) short-medium household's education and no children (short-medium/no children).

Diagnosis of type 2 diabetes

Based on the definitions by Hvidberg et al. (2016), T2D was measured by inpatient and outpatient diagnosis with the International Classification of Disease (ICD) version 10 code E11-14 and medication with the Anatomical Therapeutic Chemical Classification System (ATC) codes A10A and A10B.[24] Information on

Fig. 1. Flowchart.

diagnosis was obtained from the Danish National Patient Registry, and information on antidiabetic medication was obtained from the Danish National Prescription Registry.[22]

Death

All-cause death was identified based on information about vital status from the Danish Civil Registration System.[22] All-cause death was used as outcome because it is a well-established and valid prognostic measure.

Covariates

Sex, cohabitation, place of residence, and birth cohort were considered potential confounders. Information on the covariates was retrieved from the Danish Civil Registration System[22] one year before the adult turned 65 years (baseline) unless otherwise was specified. Cohabitation was coded as cohabitating with a partner or living alone. Based on the definition by Statistics Denmark, the place of residence was categorised as capital municipalities, big city municipalities, provincial municipalities, upland municipalities, and country municipalities.[25] This variable was included as there most likely are geographical differences in diagnosis of T2D, death, and educational attainment. Birth cohort was included as a continuous variable in the statistical analyses and was presented as a categorical variable (1935–1940, 1941–1946 and 1947–1953) in the descriptive analyses for a better overview. Information on diagnoses with or medication for other chronic diseases of the older adult was obtained between the age of 60 and 65 years and was included as a dichotomous variable (no/yes). Other chronic diseases were based on Hvidberg et al. (2016)[24] and included chronic obstructive pulmonary disease, ischaemic heart disease, heart failure, pulmonary heart disease, other cardiovascular diseases, dementia, osteoporosis, depression, Parkinson's disease, and cancer (Supplementary Table S1 shows ICD10 and ATC codes). A variable for family identification was received from the Danish Civil Registration System to identify older adults living in the same household.[22]

Statistical analysis

We defined a multistate survival model with three states for our data analysis: 65th birthday (state 1 [starting state]) diagnosis of T2D (state 2 [intermediate event]), and all-cause death (state 3 [absorbing state]). Fig. 2 illustrates the model where the boxes represent the three states, and the arrows represent the possible transitions (transitions 1, 2, and 3). All older adults started in state 1 on their 65th birthday (baseline) and could then move to either state 2 or state 3. In the model, the older adults could not move backwards, e.g. from state 2 to state 1. For the older adults who experienced two states simultaneously (1 and 3, or 2 and 3), we chose to recode the earliest state in the model (1 or 2) as one day earlier. The transition matrix from the multistate model is presented with numbers of events and percentages.

Cox proportional hazards model was applied to estimate each transition hazard (hazard ratio [HR]). The older adults were followed from their 65th birthday, and censored by emigration, death, or end of follow-up (2018-12-31), whichever came first. The multistate model was adjusted for the transition-specific covariates (sex, cohabitation, place of residence and birth cohort). In all models, we included a family identifier to account for clustering. The assumption of proportional hazards was investigated and not violated for transition 1 or 2. However, it appears that there were no differences in hazard in the very beginning of follow-up for transition 3, based on the log–log plot (Figure S1 in supplementary). We also tested for and found significant interaction between the main exposure (household's and children's education) and sex and other chronic diseases at the baseline, respectively. Hence, we performed a supplementary analysis stratified by sex and other chronic diseases.

Data management and analyses were performed in the statistical software SAS version 9.4 and R statistics version 4.1.1. The multistate model was performed using the R-package *mstate*.[26]

All analyses were tested with a significance level of 5%, and estimates are presented with 95% confidence intervals (95% CIs).

Results

Descriptive statistics

Table 1 shows the distribution of baseline characteristics for the study population. Older adults with long/short-medium, long/no children, or short-medium/no children had a higher proportion of men than older adults with long/long. Older adults with long/short-medium and long/no children had a smaller proportion living in rural municipalities than older adults with long/long. Older adults with short-medium/short-medium and short-medium/long education had a higher proportion of older adults living in rural municipalities. Older adults with long/long were the group with the highest proportion of older adults cohabiting.

During a mean follow-up time of 8.1 years (8,277,332 person-years in total), 71,580 (7.0%) individuals were diagnosed with T2D, 144,855 (14.2%) died without T2D, and 17,833 (1.7%) died with T2D (Supplementary Table S2 for the transition matrix for the multistate model) with corresponding incidence rates of 9.1 per 1000 person-years for T2D, 18.4 per 1000 person-years for death without T2D, and 45.0 per 1000 person-years for death with T2D (Supplementary Table S3 for the specific incidence rates for household's and children's education).

Associations of household's and children's highest educational attainment with type 2 diabetes and death

Fig. 3 shows the HRs and 95%CIs for the associations of household's and children's education for transitions between the study baseline (65th birthday) and T2D (transition 1), 65th birthday and death (transition 2), and T2D and death (transition 3).

Long/short-medium (HR: 1.49 [95% CI: 1.44; 1.54]) or long/no children (HR: 1.69 [95% CI: 1.61;1.78]) were associated with higher

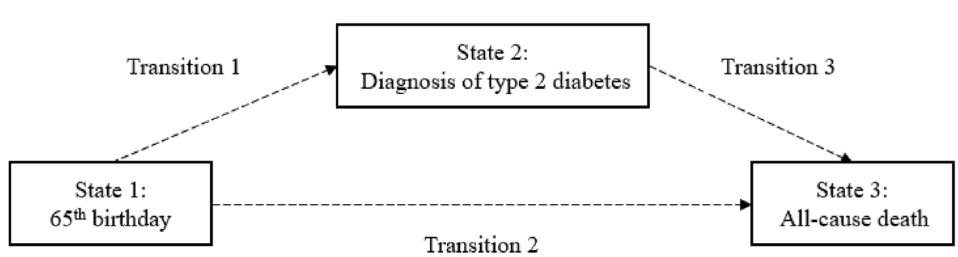

Fig. 2. Graphical presentation of the multistate survival model. Boxes represent the three states, and the arrows represent the possible transitions (transitions 1, 2, and 3).

Table 1
Baseline characteristics of the study population by household's and children's highest attainted education.

	Study population (N = 1,021,557)					
	Household's and children's highest attainted education[a]					
	Long/long n (%)	Long/short medium n (%)	Long/no children n (%)	Short-medium/long n (%)	Short-medium/ short-medium n (%)	Short-medium/ no children n (%)
	n = 126,745	n = 40,290	n = 17,577	n = 326,081	n = 393,188	n = 117,676
Sex						
Men	63,410 (50.0)	21,541 (53.5)	9540 (54.3)	142,328 (43.6)	175,973 (44.8)	67,288 (57.2)
Women	63,335 (50.0)	18,749 (46.5)	8037 (45.7)	183,753 (56.4)	217,215 (55.2)	50,388 (42.8)
Birth cohort						
1935–1940	23,927 (18.9)	9642 (23.9)	2968 (16.9)	79,726 (24.4)	124,921 (31.8)	30,617 (26.0)
1941–1946	42,601 (33.6)	14,342 (35.6)	5694 (32.4)	112,977 (34.6)	140,446 (35.7)	37,889 (32.2)
1947–1953	60,217 (47.5)	16,306 (40.5)	8915 (50.7)	133,378 (40.9)	127,821 (32.5)	49,170 (41.8)
Place of residence						
Capital municipalities	31,697 (25.0)	10,437 (25.9)	6198 (35.3)	65,183 (20.0)	79,935 (20.3)	34,430 (29.3)
Big-city municipalities	16,081 (12.7)	4409 (10.9)	1981 (11.3)	35,458 (10.9)	40,682 (10.3)	12,715 (10.8)
Provincial municipalities	29,106 (23.0)	9332 (23.2)	3365 (19.1)	78,842 (24.2)	93,447 (23.8)	24,497 (20.8)
Upland municipalities	22,730 (17.9)	7581 (18.8)	2822 (16.1)	58,626 (18.0)	74,045 (18.8)	18,015 (15.3)
Rural municipalities	27,131 (21.4)	8531 (21.2)	3211 (18.3)	87,972 (27.0)	105,079 (26.7)	28,019 (23.8)
Cohabitation status						
Cohabiting	125,283 (98.8)	39,466 (98.0)	16,716 (95.1)	235,970 (72.4)	281,105 (71.5)	47,644 (40.5)
Living Alone	1462 (1.2)	824 (2.0)	861 (4.9)	90,111 (27.6)	112,083 (28.5)	70,032 (59.5)

[a] Long/long (long household's and children's education), long/short-medium (long household's education and short-medium children's education), long/no children (long household's education and no children), short-medium/long (short-medium household's education and long children's education), short-medium/short-medium (short-medium household's and children's education), and short-medium/no children (short-medium household's education and no children).

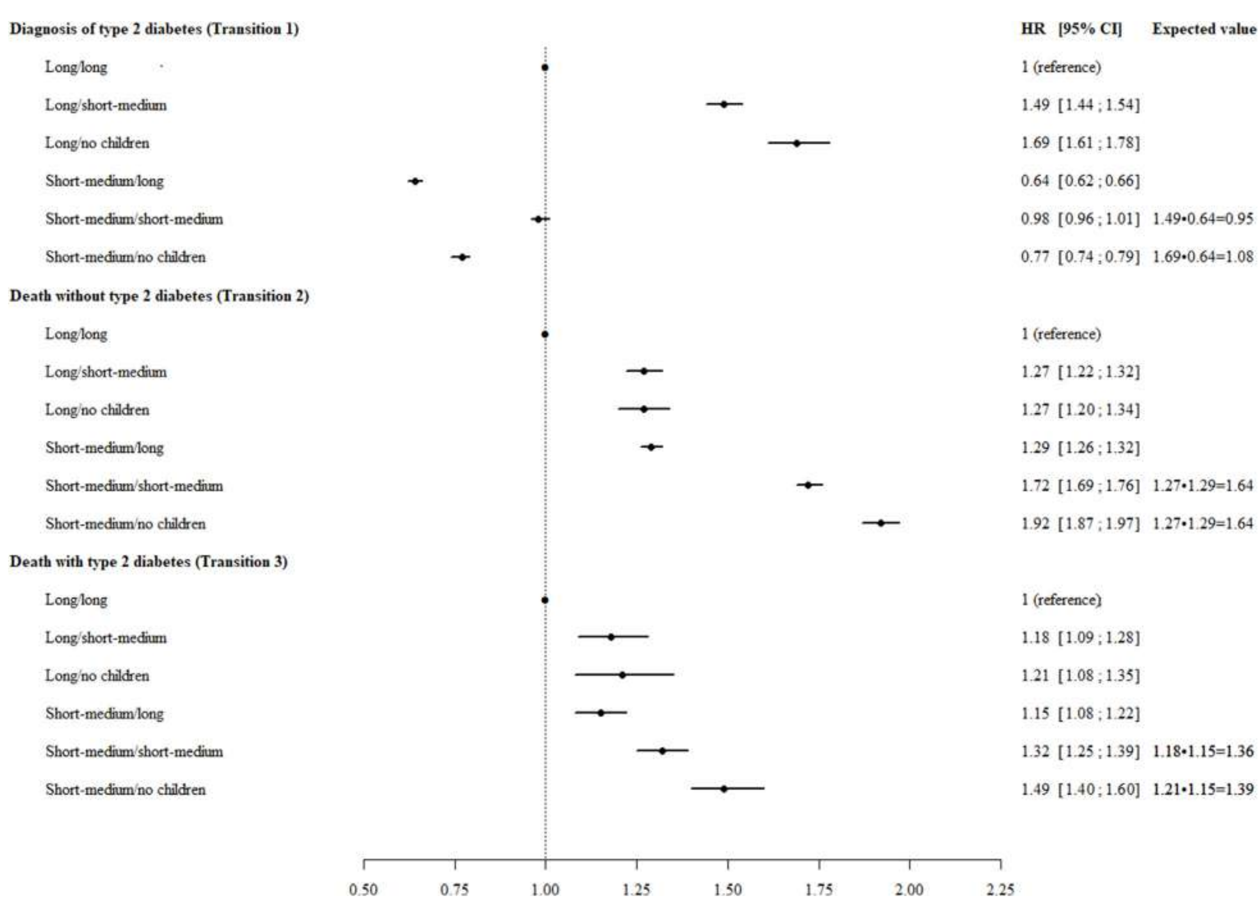

Fig. 3. Transition hazard ratios (HRs) with 95% confidence intervals [CIs] between 65th birthday, diagnosis of type 2 diabetes and death for household's and children's highest-attained education (Long/long [long household's and children's education], long/short-medium [long household's education and short-medium children's education], long/no children [long household's education and no children], short-medium/long [short-medium household's education and long children's education], short-medium/short-medium [short-medium household's and children's education], and short-medium/no children [short-medium household's education and no children]).

hazards of T2D (transition 1) than were long/long. Short-medium/long (HR: 0.64 [95% CI: 0.62; 0.66]) or short-medium/no children (HR: 0.77 [95% CI: 0.74; 0.79]) were associated with lower hazards of T2D (transition 1) than were long/long.

Compared to long/long, long/short-medium was associated with a 1.27 times (95% CI: 1.22; 1.32) higher hazard of death without T2D (transition 2) and a 1.18 times (95% CI: 1.09; 1.28) higher hazard of death with T2D (transition 3). The corresponding HRs for long/no children were 1.27 (95% CI: 1.20; 1.34) and 1.21 (95% CI: 1.08; 1.35). Short-medium/long, short-medium/short-medium, and short-medium/no children, were also associated with higher hazards of death without (transition 2) and with T2D (transition 3), than were long/long.

We identified a significant interaction between education at household level and children's education with a log-likelihood test comparing the model with and without the interaction. Compared to long/long, older adults with short-medium/no children had a lower hazard of T2D (HR: 0.77) than the expected joint effect, which is the product of the risk estimates ($1.69*0.64 = 1.08$). This expressed an antagonistic interaction on the multiplicative scale. For death without T2D, the jointed effects of short-medium/short-medium and short-medium/no children were higher than the expected joint effect. The jointed effect of short-medium/no children were also higher than the expected joint effect for death with T2D (Fig. 3). This expressed synergistic interactions on the multiplicative scale.

Supplementary analyses

We identified an interaction between the combined variable of household's and children's education and sex and other chronic diseases. However, the results were overall comparable for women and men with and without other chronic diseases; thus, these analyses are solely included in supplementary (Supplementary Table S4).

Discussion

Main findings

This study showed that among adults aged ≥65 years, those with long/short-medium or long/no children had higher hazards of T2D, whereas those with short-medium/long and short-medium/no children had lower hazards of T2D. Furthermore, we found an interaction between household's and children's education where individuals with short-medium/no children had a lower hazard of T2D than expected. Compared to long/long, all other combination of household's and children's education were associated with higher hazards of all-cause death without and with T2D. We found an interaction between household's and children's education where older adults with short-medium/short-medium had a higher hazard of death without T2D than expected, and older adults with short-medium/no children had a higher hazard of death with and without T2D than the expected joint effect.

Previous studies on the socioeconomic inequality in type 2 diabetes and death

We are not aware of previous studies investigating the association of children's education or the interplay with household's education and the risk of T2D. However, in a previous study we showed that children's socioeconomic resources were associated with higher risk of stroke in a Danish and Swedish population also followed from the of age 65 years.[27] It is likely that the same mechanisms may be at play to explain our findings for T2D: adult children with long education may have the resources and knowledge to influence and guide their parents to healthier habits such as a healthy diet and exercise,[13] which could in turn reduce their parents' risk of T2D and death. This is supported by an American study, which found that compared to having children with long education, having children with short education was associated with a higher risk of smoking and low level of physical activity.[12]

We found that older adults with short-medium/long and short-medium/no children had lower hazards of T2D, yet we had expected to identify higher hazards of T2D. Our findings could be influenced by information bias as hospital diagnoses and prescription medicine were used to identify T2D. A study from Norway found that short education was associated with a higher prevalence of undiagnosed diabetes.[28] If this is also the case in our study population, we may have underestimated the risk of T2D among older adults with short-medium household education. Also, the results could be influenced by selection because we only include older adults aged 65 years and older, whereas individuals with fewer socioeconomic resources have been found to develop T2D earlier in life[29] and die at a younger age.[30] However, when comparing the distribution of household education of the excluded older adults with T2D at the baseline (long education: 21.8%, short-medium education: 78.2%) with the study population (long education: 18.1%, short-medium education: 81.9%), we found no indication of selection bias. Yet, we did not include individuals who died prior to the age of 65 years, which may have contributed to selection bias because we would expect a larger proportion of individuals with short-medium education in this group, especially among those who had also developed T2D and died before the age of 65 years. It could also be that the association between short-medium/long and T2D is a true relationship, which could indicate that children with long education who have parents with short-medium education may be more attentive and supportive of their parents more in relation to health and thus help in preventing T2D, explaining the identified lower hazard of T2D.

Our findings regarding death are in line with previous studies of the positive impact of having children, and household's and children's socioeconomic resources, both in general populations[8,9,11–19,31–33] and populations with chronic conditions, including stroke and breast cancer.[17,34–36] Looking at the risk estimates for death, they are slightly lower for the analyses of death with T2D (transition 3) than for death without T2D (transition 2). However, the HRs for transition 3 represent greater absolute differences as the incidence rates of death with T2D (transition 3) are higher than for death without T2D (transition 2). Furthermore, we found a synergistic interaction between short-medium household's education and no children for death without (transition 2) and with T2D (transition 3), and between short-medium household's education and short-medium children's education for death without T2D (transition 2). We identified differential vulnerability of having children and their education by synergetic interaction with household's education in the hazard of death.[21] These findings showed that in case of death, the impact of not having children (for death without and with T2D) or children with short-medium education (for death without T2D) was greater for older adults with short-medium education than for older adults with long education.

Strengths and limitations

This study is based on a nationwide cohort and included all individuals born between 1935 and 1953 who turned 65 years of age, with a unique linkage between generations using Danish registers. This limited selection bias and made it possible to investigate a large cohort with complete information. Information on T2D was included based on both hospital diagnoses and redeemed prescription medicine from the Danish National Patient Register and the Danish National Prescription register. Diagnosis of T2D in the Danish National Patient Register has been identified to have a positive predictive value of 96.0 [86.5–98.9],[37] and a specificity of around 76% has been identified in the Danish National Patient Register, the National Diabetes Register, and the Danish National Prescription register when compared to HbA1c blood samples.[38] We had complete information on death from the CPR register.[22] Information on education was chosen as an indicator of children's socioeconomic resources since education is an indicator of capacity of knowledge and skills[39] and is presumed to be more stable from the age of 30 years than other socioeconomic indicators such as income and occupation. Information on the household's education was retrieved at age 64 years, yet the older adults may become widows or change partner, which could change the educational level in their household. We did not account for this, which, in case of a true association, would most likely lead to no association. As this study is observational, it is likely that the associations are influenced by unmeasured confounding, such as the importance of genetics and family environmental factors, which could be investigated in sibling or twin studies, or in personality traits that may be linked to educational level and health-related behaviour. The findings of the study might be applicable to countries similar to Denmark with a welfare state and similar family structures.

Implications for policy, practice, and research

Even though this is an observational study, which may limit causal conclusions, our findings suggest that not only the educational level of the household but also having children and their educational level have an impact on the hazard of death with and without T2D. Healthcare professionals in primary and secondary care should therefore pay attention to the level of support that the older adults receive from their children. The findings suggest that it may be relevant for healthcare professionals to offer elective interventions to the older adults who lack support from their children. Such interventions could focus on educating the patients in disease management to improve the all-cause mortality.

Furthermore, future studies could aim at detangling the complex findings regarding the hazard of diagnosis of T2D. Specifically, it would be relevant in future studies to investigate whether there is a link between having children and their educational level with underdiagnosis of T2D.

Conclusion

We found that adults with long/short-medium and long/no children were associated with higher hazard of T2D, whereas older adults with short-medium/long or short-medium/no children had lower hazard of T2D. Furthermore, we found that older adults with short-medium/no children had a lower hazard of T2D than the expected joint effect. Compared to long/long, any other combination of household's and children's education were associated with higher hazards of death both without and with T2D. Older adults with short-medium/short-medium had a higher hazard of death without T2D than expected, and older adults with short-medium/no children had a higher hazard of death both without and with T2D than the expected joint effect. This could indicate differential vulnerability, where the negative impact of having children with short-medium education or no children is more pronounced among older adults with short-medium household's education than among older adults with long household's education. Our findings could suggest that healthcare professionals should not only be aware of the level of education in the patients' household, but also on whether they have children and their educational level.

Author statements

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Ethical approval

The data are anonymised by Statistics Denmark. Thus, ethical approval is not needed for analyses of register-based data in Denmark.

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Competing interests

None declared.

Data availability

The anonymised dataset that supports the findings of this study is available from Statistics Denmark. To access the dataset, researchers need to apply to Statistics Denmark. Access is only granted for authorised research and analysis environments of a more permanent nature which has a chief researcher and several researchers or analysts. Foreign researchers who are affiliated to a Danish authorised environment can also get access.

Authors' relationships and activities

The authors declare that there are no relationships or activities that might bias or be perceived to bias their work.

Contributors

All authors have approved the final article. TSHJ, ENL and MMBS has full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analyses. Study concept: TSHJ, MO, MMBS, ENL, JN, SPA. Study design: TSHJ, MO, MMBS, ENL, JN, SPA. Acquisition of data: TSHJ. Statistical analysis: ENL and MMBS. Interpretation of results: All authors. Drafting of the manuscript: ENL. Critical revision of the manuscript for important intellectual content: All authors.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.puhe.2023.08.033.

References

1. Guariguata L, Whiting DR, Hambleton I, Beagley J, Linnenkamp U, Shaw JE. Global estimates of diabetes prevalence for 2013 and projections for 2035. *Diabetes Res Clin Pract* 2014;**103**:137–49.
2. Agardh E, Allebeck P, Hallqvist J, Moradi T, Sidorchuk A. Type 2 diabetes incidence and socio-economic position: a systematic review and meta-analysis. *Int J Epidemiol* 2011;**40**:804–18.
3. Bird Y, Lemstra M, Rogers M, Moraros J. The relationship between socioeconomic status/income and prevalence of diabetes and associated conditions: a cross-sectional population-based study in Saskatchewan, Canada. *Int J Equity Health* 2015;**14**:93.
4. Rawshani A, Svensson A-M, Zethelius B, Eliasson B, Rosengren A, Gudbjörnsdottir S. Association between socioeconomic status and mortality, cardiovascular disease, and cancer in patients with type 2 diabetes. *JAMA Intern Med* 2016;**176**:1146–54.
5. Tatulashvili S, Fagherazzi G, Dow C, Cohen R, Fosse S, Bihan H. Socioeconomic inequalities and type 2 diabetes complications: a systematic review. *Diabetes Metab* 2020;**46**:89–99.
6. Vandenheede H, Vanroelen C, Gadeyne S, De Grande H, Debossere P. Household-based socioeconomic position and diabetes-related mortality among married and cohabiting persons: findings from a census-based cohort study (Flanders, 2001–2010). *J Epidemiol Community Health* 2013;**67**:765–71.
7. Schram MT, Assendelft WJJ, van Tilburg TG, Dukers-Muijrers NHTM. Social networks and type 2 diabetes: a narrative review. *Diabetologia* 2021;**64**:1905–16.
8. Elo IT, Martikainen P, Aaltonen M. Children's educational attainment, occupation, and income and their parents' mortality. *Popul Stud* 2018;**72**:53–73.
9. De Neve J-W, Kawachi I. Spillovers between siblings and from offspring to parents are understudied: a review and future directions for research. *Soc Sci Med* 2017;**183**:56–61.
10. Zimmer Z, Hermalin AI, Lin H-S. Whose education counts? The added impact of adult-child education on physical functioning of older Taiwanese. *J Gerontol B Psychol Sci Soc Sci* 2002;**57**:S23–32.
11. Zimmer Z, Martin LG, Ofstedal MB, Chuang YL. Education of adult children and mortality of their elderly parents in Taiwan. *Demography* 2007;**44**:289–305.
12. Friedman EM, Mare R. *Education of children and differential mortality of parents: do parents benefit from their children's attainments?*. 2010. UCLA CCPR Population Working Papers, http://papers.ccpr.ucla.edu/index.php/pwp/article/view/PWP-CCPR-2010-011. [Accessed 4 February 2022].
13. Torssander J. From child to parent? The significance of children's education for their parents' longevity. *Demography* 2013;**50**:637–59.
14. Torssander J. Adult children's socioeconomic positions and their parents' mortality: a comparison of education, occupational class, and income. *Soc Sci Med* 2014;**122**:148–56.
15. Lundborg P, Majlesi K. Intergenerational transmission of human capital: is it a one-way street? *J Health Econ* 2018;**57**:206–20.
16. Yang L, Martikainen P, Silventoinen K. Effects of individual, spousal, and offspring socioeconomic status on mortality among elderly people in China. *J Epidemiol* 2016;**26**:602–9.
17. Meyer AC, Brooke HL, Modig K. The role of children and their socioeconomic resources for the risk of hospitalisation and mortality – a nationwide register-based study of the total Swedish population over the age 70. *BMC Geriatr* 2019;**19**:114.
18. Sabater A, Graham E, Marshall A. Does having highly educated adult children reduce mortality risks for parents with low educational attainment in Europe? *Ageing Soc* 2020;**40**:2635–70.
19. Cui Y, Liu H, Zhao L. Protective effect of adult children's education on parental survival in China: gender differences and underlying mechanisms. *Soc Sci Med* 2021;**277**:113908.
20. Berkman LF, Glass T. Social integration, social networks, social support, and health. *In* L F Berkman, & I Kawachi (Eds) Social epidemiology.
21. Diderichsen F, Evans T, Whitehead M. The social basis of disparities in health. In: Evans T, Whitehead M, Diderichsen F, et al. (eds) Challenging inequities in health: from ethics to action. Oxford University Press, .
22. Thygesen LC, Daasnes C, Thaulow I, Brønnum-Hansen H. Introduction to Danish (nationwide) registers on health and social issues: structure, access, legislation, and archiving. *Scand J Public Health* 2011;**39**:12–6.
23. Erikson R. Social class of men, women and families. *Sociology* 1984;**18**:500–14.
24. Hvidberg MF, Johnsen SP, Glümer C, Petersen KD, Olesen AV, Ehlers L. Catalog of 199 register-based definitions of chronic conditions. *Scand J Public Health* 2016;**44**:462–79.
25. Statistics Denmark. Kommunegrupper, v1:2018, https://www.dst.dk/da/Statistik/dokumentation/nomenklaturer/kommunegrupper (n.a., accessed 12 May 2022).
26. Putter H, Wreede LC de, Fiocco M, Geskus RB, Bonneville EF, Manevski D. *Mstate: data preparation, estimation and prediction in multi-state models*. 2021. https://CRAN.R-project.org/package=mstate. [Accessed 11 November 2022].
27. Jørgensen TSH, Osler M, Fors S, Nilsson CJ, Meyer A, Modig K. Adult offspring and their socioeconomic resources for development and survival of stroke: a Swedish and Danish nationwide register-based study. *Scand J Public Health* 2023:14034948231152352.
28. Ruiz PL-D, Hopstock LA, Eggen AE, Njølstad I, Grimnes G, Stene LC, et al. Undiagnosed diabetes based on HbA1c by socioeconomic status and healthcare consumption in the Tromsø Study 1994–2016. *BMJ Open Diabet Res Care* 2021;**9**:e002423.
29. Wilmot E, Idris I. Early onset type 2 diabetes: risk factors, clinical impact and management. *Therap Adv Chron Disease* 2014;**5**:234–44.
30. Martin LG, Preston SH. *Socioeconomic differences in adult mortality and health status*. National Academies Press (US); 1994. https://www.ncbi.nlm.nih.gov/books/NBK236675/. [Accessed 24 January 2023].
31. Högnäs RS, Roelfs DJ, Shor E, Moore C, Reece T. J-curve? A meta-analysis and meta-regression of parity and parental mortality. *Popul Res Pol Rev* 2017;**36**:273–308.
32. Modig K, Talbäck M, Torssander J, Ahlbom A. Payback time? Influence of having children on mortality in old age. *J Epidemiol Community Health* 2017;**71**:424–30.
33. Torssander J, Erikson R. Marital partner and mortality: the effects of the social positions of both spouses. *J Epidemiol Community Health* 2009;**63**:992–8.
34. Brooke HL, Ringbäck Weitoft G, Talbäck M, Talbäck M, Feychting M, Ljung R. Adult children's socioeconomic resources and mothers' survival after a breast cancer diagnosis: a Swedish population-based cohort study. *BMJ Open* 2017;**7**:e014968.
35. Meyer AC, Torssander J, Talbäck M, Modig K. Parents survive longer after stroke than childless individuals: a prospective cohort study of Swedes over the age of 65. *Eur J Public Health* 2019;**29**:1090–5.
36. Brown AF, Ettner SL, Piette J, Weinberger M, Gregg E, Shapiro MF, et al. Socioeconomic position and health among persons with diabetes mellitus: a conceptual framework and review of the literature. *Epidemiol Rev* 2004;**26**:63–77.
37. Schmidt M, Schmidt SAJ, Sandegaard JL, Ehrenstein V, Pedersen L, Sørensen HT. The Danish National Patient Registry: a review of content, data quality, and research potential. *Clin Epidemiol* 2015;**7**:449–90.
38. Jørgensen ME, Ellervik C, Ekholm O, Johansen NB, Carstensen B. Estimates of prediabetes and undiagnosed type 2 diabetes in Denmark: the end of an epidemic or a diagnostic artefact? *Scand J Public Health* 2020;**48**:106–12.
39. Cutler DM, Lleras-Muney A. Understanding differences in health behaviors by education. *J Health Econ* 2010;**29**:1–28.