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OLDER ADULTS

Making the Most of Mealtimes (M3): effect of eating occasions and other covariates on energy and protein intake among Canadian older adult residents in long-term care

V. Trinca,[1] J. Morrison,[1] S. Slaughter[2] & H. Keller[1,3]

[1]Kinesiology Department, University of Waterloo, Waterloo, Ontario, Canada
[2]Faculty of Nursing, University of Alberta, Edmonton, Alberta, Canada
[3]Research Institute for Aging, Schlegel-University of Waterloo, Waterloo, Ontario, Canada

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Correspondence
H. Keller, Kinesiology Department, University of Waterloo; Research Institute for Aging, Schlegel-University of Waterloo, Waterloo, Ontario, Canada.
Tel.: 519 904 0660 ext 4205
E-mail: hkeller@uwaterloo.ca

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Abstract

Background: Food intake varies among long-term care (LTC) residents and, as a result, some residents are at risk for protein-energy malnutrition and its consequences, such as sarcopenia. The present study aimed to determine whether eating occasions, as well as other factors that may vary with eating occasions (e.g. family/volunteer presence), were associated with energy and protein intake at meals and snacks.
Methods: The present study comprised a secondary analysis of the cross-sectional Making the Most of Mealtimes study, including 630 residents (median age 88.00 years, range 62–107 years; 197 males) from 32 Canadian LTC homes. An analysis of variance compared protein and energy intake at meals and snacks. Mixed repeated measures linear regression testing for meal and relevant covariates (e.g. family/volunteer presence) was also conducted.
Results: Energy and protein intake was significantly associated with eating occasions ($F = 44.31$, $P < 0.001$; $F = 12.72$, $P < 0.001$), with the greatest energy intake at breakfast, and the greatest protein intake at dinner. Regression analysis confirmed these findings when considering other factors. Covariates associated with higher intake included: being male (+79 kcal; +3.4 g protein), living on a dementia care unit (+39 kcal; +2.1 g protein) and family/volunteer presence at meals (+58 kcal; +2.5 g protein). Intake was lowest in the oldest age group (−59 kcal; −3.6 g protein) and for those sometimes requiring eating assistance (−36 kcal; −2.0 g protein).
Conclusions: Energy and protein intake appears to be associated with eating occasions. Based on these exploratory findings, LTC homes may consider providing more protein-dense foods at breakfast. Protein and energy dense snacks could also be used more extensively to support intake.

Introduction

A high proportion of long-term care (LTC) residents do not meet energy and protein recommendations, which can result in malnutrition [1–6], estimated to occur in approximately 30–44% of residents [1,3,5]. Protein-energy malnutrition is associated with numerous adverse health outcomes, including sarcopenia, an increased incidence of wounds, infections and falls, and a decreased quality of life [4,7–10]. Promoting food intake in residents at risk for malnutrition is an important focus for LTC providers. Foodservice strategies may promote food intake, such as providing flavours and foods appealing to residents, or more offerings at a meal [11]. The timing of meals and provision of snacks between meals is another care strategy.

Dietitians of Canada have identified that serving meals at approximately equal intervals throughout the day, with breakfast being available until at least 08.30 h, and dinner (i.e. evening meal) not being served until at least 17.00 h,

as best practices in LTC [12]. The main meal served in Canadian LTC is typically either lunch (mid-day meal) or dinner [1,13–15], with approximately two-thirds having dinner as the main meal [1]. Because main meals are typically later in the day, meals provided earlier in the day may be less energy- and protein-dense than the evening meal [15]. If food is provided more often, this may also lead to increased intake [14,15] and energy- and protein-dense snacks between meals are recommended [7,16–18]. Providing more food during the day when a resident is most interested in eating is another person-centred strategy. Yet, there is little understanding of intake with respect to various meals and snacks, as well as whether intake is significantly different across the day when considering other covariates (e.g. family/volunteer presence at meals).

Studies on eating occasions and food intake have been based on a small number of residents or homes and did not always use rigorous methods [14,15,19]. A study conducted in four Spanish LTC homes found that the largest meals served were lunch and dinner, and also that most food waste occurred during these two meals [14]. Protein intake was the greatest at lunch and dinner, whereas energy intake was highest at breakfast, and the evening snack [14]. Food intake by eating occasion has also been examined specifically in residents with dementia, where Young *et al.* (2001) found that residents with Alzheimer's consumed the most at breakfast, and least at dinner [15].

Resident characteristics will influence food intake [1,3,4,7,11,15,19–23] and may confound the relationship between eating occasions and intake. Dementia is common among LTC residents [11,20] and low food and fluid intake, as well as malnutrition, has been reported especially in this group [15,24]. Variability in activity [25], including sundowning syndrome, where residents with dementia experience increased agitation, anxiety and aggressive behaviours as the day progresses [26], may negatively influence food intake later in the day. Residents with dementia may also be more susceptible to experiencing environmental press, where factors in the environment such as noise or lighting can be considered overwhelming [27,28], resulting in behavioural expressions such as anxiety, agitation and refusing to eat [19,21,22,27,29]. Furthermore, residents with more eating challenges, including agitation are more likely to have lower intake at meals [30].

The amount and type of assistance provided greatly influences resident food intake [7,17,19,22,30,31]. In an Australian LTC home, residents who required mealtime assistance but did not receive assistance had lower protein and energy intake compared to residents who received partial or full assistance [22]. Improvements in availability and quality of assistance provided have been shown to increase energy intake during meals [17]. In some cases, greater cognitive impairment is associated with increased oral intake and better nutritional status because these residents require, and more often receive, assistance compared to residents with mild cognitive impairment or residents who do not require full assistance [22,31]. Family members who visit residents in LTC often want to be involved in meaningful interactions with the resident [32]. Providing companionship or mealtime assistance occurs with approximately 4% of family visitors [32]. Very few studies have considered whether family presence affects intake at meals. One study that investigated family assistance and resident food intake did not show a difference in intake [32].

Eating occasions may be associated with protein and energy intake and emphasising the provision of food at a specific meal is a relatively simple food service strategy to improve food intake. However, limited prior research has not accounted for confounders that also may vary with eating occasions. The present exploratory study aimed to: (i) describe protein and energy intake at various eating occasions; (ii) consider how key covariates are associated with intake at meals; and (iii) determine whether eating occasions are associated with protein and energy intake among LTC residents, at the same time as adjusting for these selected covariates.

Materials and methods

This is a secondary analysis of the Making the Most of Mealtimes (M3) cross-sectional multisite study that included 32 LTC homes from Ontario, Manitoba, New Brunswick and Alberta [20]. Convenience purposive sampling was used. Eligible LTC homes had to be operating for at least 6 months and have a minimum of 50 residents. Homes were purposively included to represent diversity in care options (i.e. profit status, client focus). Within each home, one to three units were randomly selected, although, if a dementia care unit existed in the home, that unit was included. Residents of all cognitive abilities were eligible to participate if they were over the age of 65 years (one resident was 62 years), lived in selected units for at least 1 month, ate most meals in the dining room and were not considered medically unstable or palliative. Using a random number table, eligible residents were randomly approached by trained home staff to determine interest in the study. Informed consent was completed by researchers with residents who had the capacity to provide consent; otherwise, consent was provided by an alternate decision maker, and assent was continuously evaluated throughout the data collection process [20]. Residents requiring tube feeding or if advanced directives indicated they did not wish to participate in research, were excluded. All homes had 20 residents participate in the M3 study except for one home,

where there were only 19 residents, because one resident withdrew consent [20]. Ethics review was completed at the University of Waterloo, Université de Moncton, University of Manitoba and University of Alberta.

Generally, meals were provided at the same time at each home, with breakfast being served at approximately 08.00 h, lunch at 12.00 h and dinner at 17.00 h. Food intake for meals (i.e. breakfast, lunch and dinner) was assessed using three non-consecutive days, including a weekend day by highly trained research assistants (two per home) [20]. All individual foods served on the main plate at each meal were weighed before and after consumption, and food spilled was also estimated. Intake of side dishes, snacks and beverages were estimated, with the amount consumed determined from the production menu, and from measuring vessel size. Food and beverage intake at snacks were estimated by research assistants on diet data collection days. It was determined whether the food was provided by the home or brought by the family, and what was consumed by asking the residents themselves, staff or family. Snacks were almost exclusively provided by LTC homes. Staff members were also asked to report any food or beverage intake between the evening snack and breakfast on the subsequent day. To determine the amount of protein and energy consumed, food and beverage intake was analysed using home recipes and FOOD PROCESSOR NUTRITION ANALYSIS SOFTWARE, version 10.14.1 (https://www.esha.com/products/food-processor). Research assistants worked in tandem and reviewed each other's nutrient analyses, and both data entry and analyses were checked for consistency. A detailed protocol was followed to ensure consistency in nutrient analysis across the four provinces [20]. For this analysis, 630 participants were included; those missing three or more meals out of nine, and residents who began to receive palliative care were excluded. This analysis adjusts for intra-individual variation in food intake [33,34].

The M3 study included diverse data collection at the home, unit and resident level; only those variables most relevant to adjusting for eating occasion effects within residents (e.g. eating assistance, dementia care unit) [1] and those likely to change with the meal (e.g. meal duration, presence of family/volunteers at a meal) were included. A home-level questionnaire was provided to the director of care and the food services manager in each home, recording the main meal served by the home, which was either lunch (0) or dinner (1). The main meal was defined as that where multiple components were served (e.g. an appetiser or side dishes served with an entrée and dessert) and was typically the largest offering of the day with two hot entrée options. Timing of meals and provision of snacks was also recorded on this questionnaire. The type of unit residents lived on was defined as either a general care unit (0) or dementia specific care (1). Family/volunteer presence was recorded at every meal where intake was assessed (present = 1, not present = 0). Meal duration for the unit was calculated as the time from the first item offered to the time the last food was cleared, or when the last resident left the dining room. Average time to complete meals for observed food intake days was determined for each resident. The valid and reliable 10 item Edinburgh Feeding in Dementia Scale [35] was completed at one different meal (i.e. breakfast day 1; lunch day 2; dinner day 3) for each day of food intake assessment. Items are scored as never (1), sometimes (2) or always (3; score minimum 10, maximum 30). The only item from this scale used for analyses was physical eating assistance required/received by residents. Resident cognition was measured using the Cognitive Performance Scale (CPS), which is a six-point scale [36], dichotomised for analysis (0–2 intact-mild cognitive impairment versus 3–6 moderate–severe impairment). CPS scores were derived from the interRAI Long-Term Care Facilities (LTCF; also known as Minimum Data Set) assessment [37]. The Aggressive Behavioural Scale (ABS) from the interRAI LTCF assessment was used to determine expressions of verbal and physical outbursts, resisting care and socially inappropriate or disruptive behaviours [38] and has a maximum score of 12. Each component was scored on a four-point scale (0 = behaviour not present; 1 = behaviour present but not exhibited in past 3 days; 2 = behaviour exhibited in the past 1–2 days; 3 = behaviour exhibited daily in past 3 days). Provincial research coordinators interviewed care staff currently providing care to study participants to determine CPS and ABS scores.

Statistical analysis

SAS, version 3.5 (SAS Institute Inc., Cary, NC, USA) was used to conduct analyses. For all statistical analyses, only eating occasions (i.e. meals and snacks) where residents consumed greater than 0 kcal were included. This decision was made because the dataset only included intake and not provision of food at snacks and thus refused/unconsumed snacks were not tracked. One-way analysis of variance (ANOVA) with the outcomes of energy and protein at three meals (i.e. breakfast, lunch and dinner) and three snack times (i.e. morning, afternoon and evening) determined differences in intake by eating occasion. Mean and median are reported as a result of the variability of protein and energy intake. Student's *t*-tests and one-way ANOVAs were used to determine whether covariates were associated with protein and energy intake at meals. Spearman's rho was used for continuous variables. It is important to note that intake at each eating occasion was treated as independent observations for these bivariate

analyses, and thus associations should be interpreted with caution. A fully adjusted mixed repeated measures linear regression with compound symmetry testing for meal (fixed effect) and other covariates (i.e. CPS score) determined if meal was associated with energy and protein intake. Repeated measures regression accounted for the lack of independence among eating occasions within an individual. $P > 0.05$ was considered statistically significant. Missing data were not imputed.

Results

Resident ($n = 630$) median age was 88.0 years and 31.3% of residents were male. Median CPS score was 3.0, with approximately 56% of residents with moderate to severe cognitive impairment. The 3-day median ABS score was 0. Dinner was the main meal for approximately 66% of residents. Mean (SD) energy and protein provided at meals for the regular menu were 2058 (397) kcal and 86.5 (20.7) g and 1801 (507) kcal and 82.2 (23.6) g respectively for the pureed texture diet [39]. The daily mean (SD) energy and protein intake was 1572 (412) kcal and 58.4 (18.02) g, respectively [1]. Physical eating assistance was required by approximately 22% of residents, equally distributed between sometimes and frequently, and 5% had family/volunteers present at the meal (Table 1).

Mean and median protein and energy intake for meals and snacks are provided in Table 2 and differences among meals/snacks are shown in Table 3. LTC homes were less likely to provide a morning snack (47%), as noted on the home questionnaire, whereas afternoon and evening snacks were provided in 88% of homes. Only 17% of residents consumed a morning snack, compared to 34% and 52% of residents who consumed an afternoon and evening snack, respectively. Approximately 90% of energy and protein was consumed at meals. Energy intake was significantly different by meal ($F = 44.31$, $P < 0.001$) with Tukey's post-hoc analyses demonstrating that an additional 59 kcal (247 kJ) were consumed at breakfast than lunch ($t = 8.62$, $P < 0.001$), and an additional 52 kcal (218 kJ) were consumed at breakfast than dinner ($t = 7.43$, $P < 0.001$). Energy intake was also significantly different by snack ($F = 33.56$, $P < 0.001$), with the greatest energy consumed at the evening snack. Protein intake was also significantly different by meal ($F = 12.72$, $P < 0.001$) and highest at dinner. Tukey's post-hoc analyses demonstrated that 1.4 g less protein was consumed at breakfast compared to dinner ($t = 4.57$, $P < 0.001$), and approximately 1.3 g less protein was consumed at lunch than dinner ($t = 4.00$, $P < 0.001$). Protein intake was significantly different by snack ($F = 28.06$, $P < 0.001$), with the morning snack offering the least protein, and the evening snack the most protein.

Table 1 Characteristics of residents living in long-term care ($n = 630$ residents)

Resident characteristics	Median (range)/%
Age (years)	88.00 (62.00–107.00)
Gender, male ($n = 197$)	31.27%
CPS score*	3 (0–6)
CPS score ≥3*	55.52%
ABS score†	0 (0–12)
Home-designated main meal‡	
Lunch	32.46%
Dinner	67.54%
Unit type	
Dementia care, residents	28.89%
General care, residents	71.11%
Family/volunteer present at meals§	5.30%
Requiring physical eating assistance¶	
Sometimes	10.54%
Always	11.31%
Meal duration (min)	
Breakfast**	37.00 (5.00–147.00)
Lunch††	40.00 (7.00–105.00)
Dinner‡‡	39.00 (5.00–102.00)

*CPS (Cognitive Performance Scale) scored as 0 (no impairment) to 6 (severe impairment); missing values = 5 residents.
†ABS (Aggressive Behaviour Scale) sum of three behavioural symptoms (verbal or physical abuse, socially inappropriate/disruptive behaviours, and resisting care), each score ranging from 0 to 3; missing values = 7 residents.
‡Main meal provided by the home (i.e. lunch or dinner); missing values = 20 residents.
§Family/volunteer present at meal; missing values = 150/5417 meal observations.
¶Eating assistance required; missing values = 25/5417 meal observations.
**Based on data from 1721 meal observations.
††Based on data from 1760 meal observations.
‡‡Based on data from 1764 meal observations.

Table 4 presents bivariate associations between covariates and energy and protein intake at each meal. Energy and protein intake were both significantly greater with family/volunteer presence at lunch ($t = 3.72$, $P < 0.001$; $t = 3.58$, $P < 0.001$) and dinner ($t = 4.67$, $P < 0.001$; $t = 2.49$, $P = 0.013$). Residents with greater cognitive impairment consumed significantly less protein during breakfast ($t = 2.34$, $P = 0.020$). ABS scores were not significantly correlated with energy or protein intake ($P > 0.050$). Persons living in a dementia care unit had significantly greater energy and protein intake during lunch ($t = 3.53$ $P < 0.001$; $t = 4.78$, $P < 0.001$) and dinner ($t = 4.32$, $P < 0.001$; $t = 3.62$, $P < 0.001$) compared to residents in general care units. Residents who *never* required eating assistance consumed significantly more energy and protein at breakfast ($t = 4.40$, $P < 0.001$; $t = 4.84$ $P < 0.001$) but significantly less protein during

Table 2 Energy and protein intake per meal and snack (n = 630 residents)

	Energy (kcal), mean (SD); median (range)	Protein (g), mean (SD); meedian (range)
Breakfast	526 (214);	18.4 (8.5);
	517 (3–2058)*	17.8 (0–68.4)*
Morning snack	118 (136);	2.8 (5.71);
Juice, yogurt, cookie†	71 (1–928)‡	0.4 (0–41.2)‡
Lunch	467 (196);	18.5 (9.6);
	453 (10–1394)§	17.1 (0–72.0)§
Afternoon snack	148 (110);	3.3 (4.6);
Assorted fresh fruit, muffin, cookie†	124 (1–786)¶	1.7 (0–44.6)¶
Dinner	474 (205);	19.8 (10.1);
	461 (2–1440)**	18.4 (0–71.6)**
Evening snack	187 (162);	5.0 (6.0);
Sandwiches, cookies, cheese and crackers†	140 (1–1656)††	2.9 (0–47.7)††

*Based on 1796 meal observations.
†Some examples of snacks provided during this snack occasion.
‡Based on 312 snack observations.
§Based on 1803 meal observations.
¶Based on 653 snack observations.
**Based on 1818 meal observations.
††Based on 986 snack observations.

Table 3 Differences in energy and protein intake at meals and snacks

	Energy (kcal)	*P*-value	Protein (g)	*P*-value
Breakfast versus lunch†	+59	<0.001*	−0.1	0.928
Breakfast versus dinner‡	+52	<0.001*	−1.4	<0.001*
Lunch versus dinner§	−7	0.526	−1.3	<0.001*
Morning versus afternoon snack¶	−29	0.002*	−0.5	0.302
Morning versus evening snack††	−69	<0.001*	−2.2	<0.001*
Afternoon versus evening snack‡‡	−39	<0.001*	−1.7	<0.001*

*Statistically significant ($P < 0.050$).
†Based on 1796 breakfast observations and 1803 lunch observations.
‡Based on 1796 breakfast observations and 1818 dinner observations.
§Based on 1803 lunch observations and 1818 dinner observations.
¶Based 312 morning snack observations and 653 afternoon snack observations.
††Based on 312 morning snack observations and 986 evening snack observations.
‡‡Based on 653 afternoon snack observations and 986 evening snack observations.

Table 4 Protein and energy intake contrasted by key covariates by meal

	Energy (kcal)	*P*-value	Protein (g)	*P*-value
Family/volunteer present versus not present at meal¶				
Breakfast†	+61	0.086	+1.2	0.399
Lunch‡	+64	<0.001*	+3.7	<0.001*
Dinner§	+95	<0.001*	+2.5	0.013*
CPS (3+ versus <3)††,‡‡				
Breakfast	−18	0.082	−0.9	0.020*
Lunch	−7	0.452	+0.1	0.829
Dinner	−10	0.289	−0.2	0.653
Dementia care versus General care unit§§				
Breakfast	+17	0.125	+0.8	0.069
Lunch	+36	<0.001*	+2.5	<0.001*
Dinner	+47	<0.001*	+1.9	<0.001*
Requiring physical eating assistance¶¶				
Breakfast		<0.001*		<0.001*
Never versus frequently	+65	<0.001*	+2.8	<0.001*
Never versus sometimes	+56	0.003*	+2.9	<0.001*
Sometimes versus frequently	+9	0.901	−0.0	0.999
Lunch		<0.001*		<0.001*
Never versus frequently	−36	0.067	−2.2	0.015*
Never versus sometimes	+50	<0.001*	+2.3	<0.001*
Sometimes versus frequently	−86	<0.001*	−4.7	<0.001*
Dinner		0.010*		0.001*
Never versus frequently	−17	0.516	−1.3	0.241
Never versus sometimes	+41	0.034	+2.6	<0.001*
Sometimes versus frequently	−57	0.017*	−3.9	<0.001*
Home-designated main meal (lunch versus dinner)†††				
Breakfast	−40	<0.001*	−0.5	0.261
Lunch	−16	0.099	+4.0	<0.001*
Dinner	+24	0.020*	+0.1	0.845

*Statistically significant ($P < 0.050$).
†Difference in intake when family present during breakfast; n = 36/1796 breakfast observations with family/volunteer present.
‡Difference in intake when family present during lunch; n = 136/1803 lunch observations with family/volunteer present.
§Difference in intake when family present during dinner; n = 107/1818 dinner observations with family/volunteer present.
¶Based on data from 5267 meal observations.
††CPS (Cognitive Performance Scale) scored as 0–2 (none – mild impairment), 3–6 (moderate-severe impairment).
‡‡Based on data from 5372 meal observations.
§§Based on data from 5417 meal observations.
¶¶Based on data from 5392 meal observations.
†††Based on data from 5240 meal observations.

lunch ($t = 2.78$ $P = 0.005$) compared to those who *frequently* required eating assistance. On the other hand, residents who *never* required eating assistance consumed more energy and protein at breakfast ($t = 3.33$, $P < 0.001$; $t = 4.74$, $P < 0.001$) and lunch ($t = 3.36$, $P < 0.001$; $t = 3.48$, $P < 0.001$) compared to residents who *sometimes* required eating assistance. Lastly, residents who *sometimes* required eating assistance consumed less energy and protein during lunch ($t = 4.14$, $P < 0.001$; $t = 4.93$ $P < 0.001$) and dinner ($t = 2.74$, $P = 0.017$; $t = 3.84$, $P < 0.001$) compared to residents who *frequently*

required eating assistance. When lunch was the main meal served by the home, significantly more protein was consumed at lunch ($t = 8.18$, $P < 0.001$) than dinner, but significantly more kilocalories were consumed during breakfast ($t = 3.91$, $P < 0.001$) and dinner ($t = 2.34$, $P = 0.020$) versus lunch.

Because approximately 90% of food intake occurred at meals, only meals were modelled to determine potential significant differences in energy and protein intake when considering covariates (Table 5). Breakfast had the greatest energy intake, although protein intake was significantly higher at dinner. However, when dinner was the main meal designated by the home, protein intake was lower by 1.1 g compared to when lunch was the main meal. The oldest residents (>90 years) had a lower protein intake than the reference group aged 60–69 years. Men had a significantly higher protein and energy intake compared to women. Being on a dementia care unit was associated with a higher protein and energy intake. ABS score was associated with intake, where residents with more expressions had a lower protein intake. CPS score was not associated with protein or energy intake. Family/volunteer presence during meals significantly increased energy and protein intake, whereas those who sometimes required eating assistance had lower energy and protein intake compared to those who never required eating assistance. Intake for residents who frequently required eating assistance did not significantly differ from those who required no assistance.

Table 5 Regression model based on covariates explaining variance in average protein and energy intake by meal ($n = 630$ residents)

	Energy[†]		Protein[†]	
Variable	Parameter Estimate (kcal)	*P*-value	Parameter Estimate (g)	*P*-value
Lunch[‡]	−66	<0.001*	−0.4	0.298
Dinner[‡]	−59	<0.001*	+1.1	0.008*
Sex (male versus female)	+79	<0.001*	+3.4	<0.001*
Age (70–79)[§]	+36	0.121	+0.7	0.498
Age (80–89)[§]	+13	0.549	−0.9	0.405
Age (90–99)[§]	−16	0.471	−2.2	0.036*
Age (100–109)[§]	−59	0.062	−3.6	0.013*
Main meal, dinner[¶]	+13	0.102	−1.1	0.004*
CPS score (3–6)[††]	−14	0.116	−0.3	0.477
Dementia care unit[‡‡]	+39	<0.001*	+2.1	<0.001*
ABS score[§§]	−2	0.228	−0.1	0.027*
Family/volunteer present at meal	+58	<0.001*	+2.5	<0.001*
Requiring physical eating assistance (sometimes versus never)[¶¶]	−36	0.003*	−2.0	<0.001*
Requiring physical eating assistance (frequently versus never)[¶¶]	−4	0.749	−0.2	0.708

*Statistically significant ($P < 0.050$).
[†]Based on 5016/7368 meal observations. 2352 meal observations excluded as a result of missing data.
[‡]Compared to breakfast.
[§]Compared to age category 60–69.
[¶]Compared to lunch.
[††]CPS (Cognitive Performance Scale) scored as 0–2 (none – mild impairment), 3–6 (moderate-severe impairment).
[‡‡]Comparing to general care units.
[§§]Change in energy and protein consumption for every 1-point increase on ABS (Aggressive Behaviour Scale); sum of three behavioural symptoms (verbal or physical abuse, socially inappropriate/disruptive behaviours, and resisting care), each score ranging from 0 to 3).
[¶¶]Compared to never requiring eating assistance.

Discussion

The present study aimed to determine whether food intake is associated with eating occasion. As noted in the prior analysis of these data, protein intake is typically below [(8)] the recent recommendations of 1.2 g kg^{-1} body weight [(40)]. The present study identified that eating occasions and the types of food offered at different eating occasions may be a relevant mechanism for promoting food intake in some LTC residents. Energy and protein intake of residents in LTC was significantly associated with eating occasions in this analysis. Residents consumed the most energy at breakfast and the evening snack, as well as the most protein during dinner and the evening snack; these findings are consistent with prior work [(14,15)]. Energy intake continued to be highest at breakfast when adjusting for other covariates and was an important factor in the variability of energy intake when compared with covariates (i.e. based on effect size of kcal) (Table 5) and corroborates prior research where adjusting for other resident and home characteristics was not undertaken [(14,15)]. Higher energy intake at breakfast may be attributed not only to hunger as a result of the long overnight fast, but also residents being well rested. Protein intake was highest at dinner (i.e. evening meal) and continued to be significantly higher in multivariate regression analysis. However, unlike energy, this regression identified that age, sex, family/volunteer presence, requiring eating assistance and living on a dementia care unit may be more relevant for protein intake than eating occasion (Table 5). Furthermore, it was noted that, when the evening meal was the home designated main meal of the day, protein intake slightly decreased compared to when lunch was the main meal. Spreading protein out through the day rather than emphasising a single meal is a potential strategy to support higher protein intake in LTC.

Regularly providing between meal snacks may also increase the protein and energy intake of residents [(7)]. As

noted in this analysis, many residents did not consume snacks, with most residents consuming food at the evening, and the least at the morning snack. More than half of the homes did not offer a morning snack, whereas an afternoon and evening snack occurred in almost all homes. This may be a result not only of food and labour costs, but also recognition that breakfast and lunch are closer together (approximately 3–4 h), whereas the time between dinner and breakfast is more than 12 h. The morning and afternoon snack is often a cookie, portion of fruit, or yogurt, whereas the evening snack may include a glass of milk, half-sandwich or crackers and cheese. This analysis suggests that there is opportunity to increase protein intake by distributing protein more evenly across all three meals, especially breakfast, and, where feasible from a labour and food cost perspective, providing food offerings at snacks with protein.

Some covariates were associated with increased intake, although they are also associated with eating occasions. This is the first time covariates by eating occasion have been examined to determine potential variance across the day (Table 4). This analysis provides new insight and encourages providers to take a person-centred approach to resolving low intake in residents. Consistent with prior work [32], family/volunteer presence during meals promoted intake, although this was relatively infrequent, occurring for approximately 5% of residents. Family/volunteer presence at dinner resulted in significantly greater intake, especially of energy (Table 4), potentially as this was the main meal. However, protein intake was highest when family/volunteers supported lunch, suggesting that they especially encouraged intake of high protein foods at this meal. Supporting family/volunteers to provide eating assistance should be the objective of future work. Those who sometimes required eating assistance had lower protein and energy intake when other covariates were considered compared to those who never required eating assistance. The level of physical eating assistance was significantly associated with each meal for energy and protein intake in bivariate analyses, although the size of effect varied. Greatest differences in intake were seen at lunch (Table 4) for residents who sometimes versus frequently required physical eating assistance, with those who sometimes required assistance consuming 86 kcal less. Further exploration on why this occurred is necessary, especially because sundowning (e.g. more expressions in the evening) would not explain this effect. Cognitive impairment is often associated with poor food and fluid intake [15], and more behavioural expressions such as refusal to eat, and wandering [22], especially in the absence of appropriate assistance [30,31]. In multivariate analysis, greater cognitive impairment was not significantly associated with protein or energy consumption, potentially because other covariates associated with dementia were included in the analysis and had a significant effect (e.g. dementia care unit, requiring eating assistance, etc.). This may also be a result of the categorisation of CPS scores (<3 and 3+) for this analysis, as well as the crudity of the measure itself. However, behavioural expressions were significantly associated with reduced protein but not energy intake. Previous studies have found that residents with dementia have a greater desire for foods that are sweet, or carbohydratedense [21,32,39], which will increase energy consumption but possibly compromise protein intake. Therefore, further efforts to promote protein intake among this population may be needed. As noted in this analysis, living in a dementia care unit can mitigate some of these challenges, with both lunch and dinner intakes being significantly higher (Table 4). Greater staff training, and more person-centred care practices may explain differences between unit type because staff may be more attentive to the need for eating assistance or encouragement during mealtimes. One study previously found that residents living in a dementia care unit had greater protein and energy intake [1]; staff may also potentially provide more eating opportunities (i.e. snacks) to increase food intake [7].

Limitations

Although the present study included a large and diverse sample and completed a comprehensive analysis, including analysing previously unexplored covariates, there are some limitations to this work. Care plans of residents were not reviewed, and thus it is unknown whether specific strategies were being employed to facilitate food intake (e.g. larger portions, more food at breakfast) at different eating occasions. This analysis was exploratory. In the analyses, only eating occasions where residents consumed greater than 0 kcal were included, which may inflate the average intake at meals and snacks. For some covariates, proportions experiencing the factor were low (e.g. total number of meals where family was present) and other covariates were not included (e.g. use of modified texture food), aiming to provide a parsimonious, focused model. Future studies are required to confirm these associations identified in multivariate analyses. This analysis does, however, provide some opportunity to consider new interventions to promote intake. For example, making it easy for family to visit during meals and training them on foods to emphasise when assisting, may promote intake.

There are also several limitations associated with measuring the outcome of food intake. Researchers assessed intake using the best possible methods for this setting. However, 3 days of intake likely do not fully represent the usual intake of all residents. Intake may be overestimated as a result of the effects of being observed, as well as the

estimation for snacks, beverages and side dishes [38]. Although efforts were made to differentiate items for post-consumption weighing, there were challenges with respect to differentiating food items for modified texture diets where food products were mixed. Home recipes may not have represented food content, and, at best, nutrient analysis is an estimation. Accordingly, although differences in intake by eating occasions and other covariates were statistically significant in this analysis, this does not mean that these differences in intake are also clinically significant. Some differences identified were small and variability in intake and/or inaccuracies in data collection could explain some statistically significant differences. Finally, we only had consumption in the dataset, rather than what was both provided and consumed; thus, it is unknown whether a resident refused/did not consume foods or beverages, or whether they were not provided. These results cannot be generalised to other Canadian and global LTC populations because this was a convenience sample.

Conclusions

The present study investigated how eating occasions are associated with protein and energy intake among LTC residents when important covariates are considered. The data collection and analysis have demonstrated, for the first time, the relevance of eating occasions to intake when accounting for other variables such as eating assistance and family/volunteer presence. Furthermore, it is noted that the association between several covariates and intake vary by eating occasion (e.g. family/volunteer presence, requiring assistance). Energy intake was highest at breakfast and the evening snack, whereas protein was highest at dinner and the evening snack. Based on these results, LTC homes could emphasise protein content at breakfast and offer protein at snacks to improve energy and protein intake for those residents who are at risk for malnutrition.

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Conflict of interests, source of funding and authorship

The authors declare that they have no conflicts of interest.

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VT and HK conceived the study. VT conducted all of the analyses. JM provided statistical consultation and oversight. SS provided guidance on the concept. VT wrote the first draft of the paper that was reviewed and edited by all authors. All authors critically reviewed the manuscript and approved the final version submitted for publication.

Transparency declaration

The lead author affirms that this manuscript is an honest, accurate and transparent account of the study being reported. The reporting of this work is compliant with STROBE guideline. The lead author affirms that no important aspects of the study have been omitted and that any discrepancies from the study as planned have been explained.

References

1. Keller HH, Carrier N, Slaughter SE *et al.* (2017) Prevalence and determinants of poor food intake of residents living in long-term care. *J Am Med Dir Assoc* **18**, 941–941.
2. Engelheart S & Akner G (2015) Dietary intake of energy, nutrients and water in elderly people living at home or in nursing home. *J Nutr Health Aging* **19**, 265–272.
3. Lengyel C, Whiting S & Zello G (2008) Nutrient inadequacies among elderly residents of long-term care facilities. *Can J Diet Pract Res* **69**, 82–88.
4. Crogan N & Pasvogel A (2003) The influence of protein-calorie malnutrition on quality of life in nursing homes. *J Gerontol A Biol Sci Med Sci* **58**, M159–M164.
5. Mila R, Abellana R, Padro L *et al.* (2012) High consumption foods and their influence on energy and protein intake in institutionalized older adults. *J Nutr Health Aging* **16**, 115–122.
6. Morley J (2012) Do frail older persons need more protein? *J Am Med Dir Assoc* **13**, 667–668.
7. Nieuwenhuizen W, Weenen H, Rigby P *et al.* (2010) Older adults and patients in need of nutritional support: review of current treatment options and factors influencing nutritional intake. *Clin Nutr* **29**, 160–169.
8. Lam I, Keller H, Duizer L *et al.* (2015) Micronutrients on the menu: enhancing the quality of food in long-term care for regular, nontherapeutic menus. *Can J Diet Pract Res* **76**, 86–92.
9. Viveky N, Billinsky J, Thorpe L *et al.* (2013) Challenges in planning long-term care menus that meet dietary recommendations. *Can J Diet Pract Res* **74**, 84–87.
10. Ahmed T & Haboubi N (2010) Assessment and management of nutrition in older people and its importance to health. *Clin Interv Aging* **9**, 207–216.
11. Best RL & Appleton KM (2011) Comparable increases in energy, protein and fat intakes following the addition of

seasonings and sauce to an older person's meal. *Appetite* **56**, 179–182.
12. Dietitians of Canada (2017) Best Practices for Nutrition, Food Service and Dining in Long Term Care Homes. Available at: https://www.dietitians.ca/Downloads/Public/2013-Best-Practices-for-Nutrition,-Food-Service-an.aspx (accessed November 2018).
13. Ducak K & Keller H (2011) Menu planning in long-term care: toward resident centred menus. *Can J Diet Pract Res* **72**, 83. https://doi.org/10.3148/72.2.2011.83.
14. Villarroel M, Abellana Sangra R, Massaguer P *et al.* (2012) Assessment of food consumption, energy and protein intake in the meals offered in four Spanish nursing homes. *Nutr Hosp* **27**, 914–921.
15. Young K, Binns M & Greenwood C (2001) Meal delivery practices do not meet needs of Alzheimer patients with increased cognitive and behavioural difficulties in a long-term care facility. *J Gerontol A Biol Sci Med Sci* **56A**, M656–M661.
16. Dahl W, Whiting S & Robert T (2007) Protein content of pureed diets: implications for planning. *Can J Diet Pract Res* **68**, 99–102.
17. Simmons S, Hollingsworth E, Long E *et al.* (2017) Training nonnursing staff to assist with nutritional care delivery in nursing homes: a cost-effectiveness analysis. *J Am Geriatr Soc* **65**, 313–322.
18. Silver H (2008) Oral strategies to supplement older adults' dietary intakes: comparing the evidence. *Nutr Rev* **67**, 21–31.
19. Reed P, Zimmerman S, Sloane P *et al.* (2005) Characteristics associated with low food and fluid intakes in long-term care residents with dementia. *Gerontologist* **45**, 74–80.
20. Keller H, Carrier N, Slaughter S *et al.* (2017) Making the Most of Mealtimes (M3): protocol of a multi-centre cross-sectional study of food intake and its determinants in older adults living in long term care homes. *BMC Geriatr* **17**, 15.
21. Durnbaugh T, Haley B & Roberts S (1996) Assessing problem feeding behaviours in mid-stage Alzheimer's disease. *Geriatr Nurs* **17**, 63–67.
22. Nowson C, Sherwin A, McPhee J *et al.* (2003) Energy, protein, calcium, vitamin D and fibre intakes from meals in residential care establishments in Australia. *Asia Pac J Clin Nutr* **12**, 172–177.
23. Greenwood C, Tam C, Chan M *et al.* (2005) Behavioural disturbances, not cognitive deterioration, are associated with altered food selection in seniors with Alzheimer's disease. *J Gerontol A Biol Sci Med Sci* **60**, 499–505.
24. Soltesz K & Dayton J (1995) The effects of menu modification to increase dietary intake and maintain weight of Alzheimer residents. *Am J Alzheimers Dis Other Demen* **10**, 20–23.
25. Murphy J, Holmes J & Brooks C (2017) Measurements of daily energy intake and total energy expenditure in people with dementia in care homes: the use of wearable technology. *J Nutr Health Aging* **21**, 927–932.
26. Cipriani G, Lucetti C, Carlesi C *et al.* (2015) Sundown syndrome and dementia. *Eur Geriatr Med* **6**, 375–380.
27. Smith M, Gerdner L, Hall G *et al.* (2004) History, development and future of the progressively lowered stress threshold: a conceptual model for dementia care. *J Am Geriatr Soc* **52**, 1755–1760.
28. Iuglio S (2017) *Dining Environments in Long Term Care: Prevalence of Features and Construct Validity of Two Measures*. Waterloo, Ontario: UWSpace
29. Morley J (1998) Protein-energy malnutrition in older subjects. *Proc Nutr Soc* **57**, 587–592.
30. Schell E & Kayser-Jones J (1999) The effect of role-taking ability on caregiver-resident mealtime interaction. *Appl Nurs Res* **12**, 38–44.
31. Simmons S & Schnelle J (2004) Individualized feeding assistance care for nursing homes residents: staffing requirements to implement two interventions. *J Gerontol A Biol Sci Med Sci* **59A**, 966–973.
32. Durkin D, Shotwell M & Simmons S (2014) The impact of family visitation on feeding assistance quality in nursing homes. *J Appl Gerontol* **33**, 586–602.
33. National Research Council (1986) *Nutrient Adequacy: Assessment Using Food Consumption Surveys*. Washington, DC: National Academy Press.
34. Stockdell R & Amella E (2008) How to try this: the Edinburgh Feeding Evaluation in Dementia Scale. *Am J Nurs* **108**, 46–55.
35. Morris JN, Fries BE, Mehr DR *et al.* (1994) MDS cognitive performance scale. *J Gerontol* **49**, M174–M182.
36. Hirdes JP, Ljunggren G, Morris JN *et al.* (2008) Reliability of the interRAI suite of assessment instruments: a 12-country study of an integrated health information system. *BMC Health Serv Res* **8**, 277.
37. Pearlman CM & Hirdes JP (2008) The Aggressive Behaviour Scale: a new scale to measure aggression based on the Minimum Data Set. *J Am Geriatr Soc* **56**, 2298–2303.
38. Vucea V, Keller H, Morrison J *et al.* (2017) Nutritional quality of regular and pureed menus in Canadian long term care homes: an analysis of the Making the Most of Mealtimes (M3) project. *BMC Nutr* **3**, 80.
39. Nowson C & O'Connell S (2015) Protein requirements and recommendations for older people: a review. *Nutrients* **7**, 6874–6899.
40. Keene J & Hope T (1997) Hyperphagia in dementia: 2. Food choices and their macronutrient contents in hyperphagia, dementia and ageing. *Appetite* **28**, 167–175.

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OLDER ADULTS

Concurrent and predictive validity of the Mini Nutritional Assessment Short-Form and the Geriatric Nutritional Risk Index in older stroke rehabilitation patients

S. Nishioka,[1,2,3] K. Omagari,[2] E. Nishioka,[4] N. Mori,[4] Y. Taketani[3] & J. Kayashita[5]

[1]Department of Clinical Nutrition and Food Services, Nagasaki Rehabilitation Hospital, Nagasaki, Japan
[2]Graduate School of Human Health Science, University of Nagasaki, Nagasaki, Japan
[3]Department of Clinical Nutrition and Food Management, Institute of Biomedical Sciences, Tokushima University Graduate School, Tokushima, Japan
[4]Department of Clinical Services, Nagasaki Rehabilitation Hospital, Nagasaki, Japan
[5]Department of Health Sciences, Faculty of Human Culture and Science, Prefectural University of Hiroshima, Hiroshima, Japan

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Correspondence
S. Nishioka, Department of Clinical Nutrition and Food Services, Nagasaki Rehabilitation Hospital, 4-11 Gin-ya machi, Nagasaki, Nagasaki 850-0854, Japan.
Tel.: +81 95 818 2002
Fax: +81 95 821 1187
E-mail: shintacks@yahoo.co.jp

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Abstract

Background: Malnutrition may worsen clinical outcomes in stroke patients. Few malnutrition screening tools have been validated in the rehabilitation setting. The present study aimed to assess the concurrent and predictive validity of two malnutrition screening tools.
Methods: We retrospectively collected scores for the Mini Nutritional Assessment Short-Form (MNA-SF) and the Geriatric Nutritional Risk Index (GNRI) in consecutive stroke patients aged ≥65 years in a rehabilitation hospital. Concurrent validity was confirmed against the European Society for Clinical Nutrition and Metabolism diagnostic criteria for malnutrition (ESPEN-DCM). Malnutrition risk within the ESPEN-DCM process was assessed using the Malnutrition Universal Screening Tool. Cut-off values with maximum Youden index, and with sensitivity (Se) >90% and specificity (Sp) >50%, were defined as appropriate for identification and screening of malnutrition, respectively. The Functional Independence Measure and discharge destination were used to explore predictive validity.
Results: Overall, 420 patients were analysed. Of these, we included 125 patients in the malnutrition group and 295 in the non-malnutrition group based on the ESPEN-DCM. Cut-off values for the identification and screening of malnutrition were 5 (Se: 0.78; Sp: 0.85) and 7 (Se: 0.96; Sp: 0.57) for the MNA-SF; 92 (Se: 0.74; Sp: 0.84) and 98 (Se: 0.93; Sp: 0.50) for the GNRI, respectively. The GNRI predicted discharge to acute care hospital, whereas the MNA-SF did not predict all outcome measures.
Conclusions: The MNA-SF and the GNRI have a fair concurrent validity in stroke patients, although lower cut-off values than currently used were required for the MNA-SF. The GNRI exhibits good predictive validity for discharge destination.

Introduction

Individuals with stroke often experience malnutrition, with a prevalence of up to 62% [(1)]. The prevalence of malnutrition in rehabilitation hospitals/facilities is threefold higher than that in acute care hospitals [(2)]. Undernutrition leads to diminished recovery of physical and swallowing function, decreased survival rate, prolonged hospital stay and inflated healthcare costs [(3–6)]. Nutritional improvement in stroke patients with malnutrition is associated with the resumption of activities of daily living [(7,8)]. Thus, early screening and identification of malnutrition in stroke rehabilitation patients could facilitate appropriate nutritional intervention, which is necessary to

regain functional capacity and activities of daily living, as well as to improve quality of life.

Despite the growing awareness of malnutrition, malnutrition screening tools have rarely been validated specifically for stroke patients [1]. The Malnutrition Universal Screening Tool (MUST) [9] is the only malnutrition screening tool that has been used to assess predictive validity [5]; thus, its use is recommended in the recent clinical guidelines of the European Society for Clinical Nutrition and Metabolism (ESPEN) [10]. Although there is no gold standard for determining malnutrition, ESPEN has proposed operative, diagnostic criteria for malnutrition (ESPEN-DCM) [11], which are in good agreement with MUST [12]. However, to date, no study has investigated the concurrent validity of available malnutrition screening tools in stroke survivors.

The Mini Nutritional Assessment Short Form (MNA-SF) is one of the most widely used tools for the screening of malnutrition in older adults, whereas the MNA is used as an assessment tool for those identified as at risk of malnutrition [13,14]. Although the MNA-SF has shown good concurrent and predictive validity, it potentially overestimates the prevalence of malnutrition in older rehabilitation patients with a prevalence of 92%–99% being reported [3,15]. This may be attributed to non-nutrition related problems that are difficult to differentiate from characteristics of malnutrition in rehabilitation patients, including diminished physical function caused by hemiparesis, communication disorders as a result of aphasia and unintentional muscle atrophy following stroke [3]. As an alternative, the Geriatric Nutritional Risk Index (GNRI) could be useful to estimate the survival of or clinical complications in older patients [16]. In addition, the efficacy of the GNRI in estimating activities of daily living, discharge home, and recovery of full oral intake in patients with stroke have been reported [6,7,17,18]. It must be noted, however, that the GNRI indicates malnutrition risk not nutritional status because it has not been validated as a malnutrition assessment tool [19].

The present study aims to: (i) evaluate the concurrent validity of the MNA-SF and the GNRI against the ESPEN-DCM in older individuals with stroke in the convalescent stage; (ii) determine the cut-off values that correspond to and are appropriate for screening for malnutrition as defined by the ESPEN-DCM; and (iii) evaluate the predictive validity of both tools against the Functional Independence Measure (FIM) and discharge destination.

Materials and methods

We conducted this retrospective, observational cohort study in three convalescent rehabilitation wards of a single hospital in Japan. A multidisciplinary rehabilitation team provided a comprehensive rehabilitation service, which was covered by the public healthcare insurance [20]. The multidisciplinary team was composed of medical doctor, nurse, physical therapist, occupational therapist, speech-language-hearing therapist, social worker, registered dietitian, care worker and dental hygienist. This study protocol complied with the principles outlined in the Declaration of Helsinki and was approved by the Ethics Committee of the University of Nagasaki (approval number: 287) and Nagasaki Rehabilitation Hospital. Because we used only routinely collected clinical data, we supplied information about this study to all patients and explained the opt-out option, allowing patients to withdraw from the study dataset at any time.

Data source and selection criteria

In the present study, we analysed the clinical data of consecutive patients aged ≥65 years who were admitted to the convalescent rehabilitation wards for post-stroke rehabilitation from 16 May 2015 to 16 May 2017. All participants were Asian and were transferred from acute care hospitals. The exclusion criteria were: (i) missing data for serum albumin concentration within 7 days of the day of admission; (ii) no definitive diagnosis of the stroke type; and (iii) unclear data for usual body weight. The usual body weight of older stroke patients was often unavailable due to unconsciousness, aphasia, dementia or lack of routine measurement in their home. Certain patients could be classified into the malnutrition or non-malnutrition categories by the ESPEN-DCM without body weight loss and were therefore included in the analysis: (i) those patients with a body mass index (BMI) or fat-free mass index (FFMI) above the cut-off value of one of the criteria of the ESPEN-DCM but who had missing data for usual body weight (classified into non-malnutrition category) and (ii) those patients with a BMI <18.5 kg m^{-2} for whom usual body weight could not be obtained (classified into malnutrition category).

We retrospectively extracted all data from a medical chart or from the facility's data set that were entered by a registered dietitian or a medical secretary. The basic characteristics of patients collected were: age, sex, number of days from stroke onset to the date of hospital admission, length of hospital stay, stroke subtype (e.g. cerebral infarction, intracranial haemorrhage or subarachnoid haemorrhage), disabilities, comorbidities, history of stroke onset and need for long-term care before stroke. Stroke subtype, comorbidities and disabilities were diagnosed by the medical staff in the acute care hospitals or in the convalescent rehabilitation ward. The need for long-term care was verified by the medical secretary based on the

certification of the long-term care insurance (LTCI) before a stroke. The LTCI is a public, universal, long-term care insurance system in Japan [21]. At the time of admission, the nursing staff measured the body weight using a well-calibrated scale (Barrier Free Scale, A&D Co. Ltd, Tokyo, Japan) that could weigh the patients on the wheelchair. Usual body weight and body weight change were assessed by the registered dietitian based on interview with the patients and/or their representative, or from the information from the acute care hospital from where they were transferred. The nursing staff measured the height of the patients using a stadiometer or tape. If these methods could not be applied because of marked contracture of the limbs or humpback, the knee height was measured by a knee height caliper and height was calculated using a race-specific equation [22]. Both knee height measurement and height calculation were carried out by the registered dietitian. All anthropometric measures and estimations of weight history were performed on the day of admission as part of usual clinical practice.

Types of validity investigated

In the present study, we assessed concurrent validity and predictive validity. Concurrent validity demonstrates the accuracy between a screening tool (index test) and the gold standard method (reference standard) [23]. To test the concurrent validity, we divided all participants into the malnutrition group (M) and non-malnutrition group (non-M) based on the results of the ESPEN-DCM. Then, we plotted the receiver-operating characteristic curves by using the MNA-SF and GNRI to define malnutrition and evaluated the area under the curve. The maximum Youden index [sensitivity (Se) + specificity (Sp) − 1] [25]was considered as the appropriate value for identifying malnutrition. This approach is accepted to determine the cut-off value that coincides with the reference standard test. Ascertaining high sensitivity may be more important than balancing sensitivity and specificity because overlooking malnourished patients should be avoided in a clinical setting. A proposed criterion for 'good' sensitivity is >0.8, whereas 'fair' specificity is >0.5 [25]. Therefore, we set the value with >0.9 for sensitivity and >0.5 for specificity, which might be appropriate screening for malnutrition and to prevent overlooking potential patients with malnutrition. Furthermore, we used the following criteria to assess the overall capacity of each screening tool as well as kappa value (κ): good (both Se and Sp: >0.8), fair (either Se or Sp: <0.8; both Se and Sp: >0.5) and poor (either Se or Sp: <0.5) [25].

Predictive validity indicates the ability of a screening tool to predict specified outcomes [23]. Mortality, complication rate and/or length of hospital stay are usually used as outcome measures for predictive validity; several studies have also employed functional decline or discharge destination as outcome measures [25].

Outcome variables

We used two outcome measures to test predictive validity: (i) the FIM at discharge, as an indicator of activities of daily living (ADL) and (ii) discharge destination (home, long-term care facilities or hospitals/acute care hospitals). The FIM is one of the leading indicators of ADL [26], which comprises 18 domains (13 motor domains and five cognitive domains) and each domain is scored between 1 (total assistance) and 7 (complete independence). The total FIM score ranges from 18 to 126. We classified the individual data by using the ESPEN-DCM (M and non-M groups), MNA-SF and GNRI (based on the predetermined cut-off value for detecting and screening for malnutrition) and compared the outcome measures between the groups.

Index tests

We used the MNA-SF and GNRI, which are incorporated into usual clinical practice as index tests. The MNA-SF is the malnutrition screening tool that exhibits good agreement with MNA and sufficient reliability in older individuals [13,27]. The MNA-SF comprises six domains including appetite loss, weight loss, mobility, stress/acute disease, neuropsychological problems and BMI. The total score for the MNA-SF ranges from 0 to 14 points; a score of 0–7 signifies malnourished, 8–11 at risk of malnutrition and 12–14 denotes well-nourished [13]. Trained registered dietitians scored the MNA-SF on the day of admission. The components of MNA-SF that were collected are: height and body weight (used for calculating BMI); decreased food intake; change in body weight; physical and mental stress (confirmed by the patients or their representative on the day of admission, as well as relevant information provided by the acute care hospital); neuropsychological problems (evaluated by interview with patients and information from other healthcare professionals including medical doctor, nurse and occupational therapist).

The GNRI is a nutritional risk indicator for older individuals, which has been developed from the Nutritional Risk Index [28]. The equation of the GNRI is:

$$\text{GNRI} = [1.489 \times \text{albumin (g/L)}] + \{41.7 \times [\text{body weight (kg)}/\text{ideal body weight (kg)}]\}$$

Although the Lorenz formula was used for evaluating ideal body weight in the original equation of GNRI, this equation has not been validated in the Asian population.

Instead, in the present study we used BMI (22 kg m^{-2}) for determination of ideal body weight because it showed good correlation with ideal body weight calculated using the Lorenz formula in Japanese patients [29]. If the actual body weight exceeded the ideal body weight, the ratio of the body weight to the ideal body weight was set as 1. The malnutrition risk is defined by the GNRI as: severe/moderate risk, <92; low risk, 92–98; no risk, >98 [16,30]. Albumin, a component of GNRI, was assessed by attending physicians within several days from admission as a part of usual clinical practice. At admission, the registered dietitian recorded the value of serum albumin concentration and body weight in the facility's database; thereafter, the GNRI was automatically calculated using data on serum albumin, body weight, and ideal body weight.

Reference standard

In the absence of a gold standard to diagnose malnutrition, the present study used the ESPEN-DCM as the reference diagnostic standard. The consensus-based ESPEN-DCM criteria were proposed by ESPEN to diagnose malnutrition [11], are in good agreement with MUST [12] and predict survival and functional outcomes [31,32]. The criteria comprised two alternative ways to define malnutrition in patients at risk of malnutrition screened by a validated tool: (i) BMI <18.5 kg m^{-2}; and (ii) unintentional body weight loss (>5% over 3 months or >10% over an indefinite period) and low BMI (<20 kg m^{-2} for individuals aged <70 years or <22 kg m^{-2} for those aged ≥70 years) or low FFMI (<15 kg m^{-2} for females; <17 kg m^{-2} for males). FFMI can be calculated by fat-free mass (kg) divided by height $(m)^2$.

We used MUST for malnutrition screening in the ESPEN-DCM process to avoid incorporation bias. An experienced registered dietitian, who was not involved in the scoring of the MNA-SF and GNRI, performed the MUST screening and followed the diagnostic process of the ESPEN-DCM based on the nutritional information in the medical chart. The registered dietitian identified malnutrition without knowing the score of the MNA-SF and GNRI for each patient. Because body composition was not assessed in our facilities during the study period, we used the estimated fat-free mass (eFFM) based on the estimated creatinine excretion rate (eCER) for calculating FFMI [33,34]:

$$\text{eCER} = 879.89 + [12.51 \times \text{body weight (kg)}] + (6.19 \times \text{age}) + (34.51 \text{ if black}) - (379.42 \text{ if female})$$

$$\text{eFFM (kg)} = 13.0 + 0.03 \times \text{eCER}$$

$$\text{estimated FFMI (eFFMI, kg/m}^2) = \text{eFFM/height (m)}^2$$

As noted above, of all patients with missing data for usual body weight, those who showed BMI or estimated FFMI (eFFMI) above the cut-off values of ESPEN-DCM, or those with BMI <18.5 kg m^{-2} were included in the analysis, and their MUST results were expressed as 'uncertain'.

Sample size calculation

We evaluated the sample size using:

$$\text{Sample size } (N) = 4\, Z_\alpha^2 P\,(1-P)/W^2$$

where Z_α is the standard normal deviate, P is the expected sensitivity of the MNA-SF and W is the width of the confidence interval (CI).

In the present study, we set the sensitivity of the MNA-SF at 85%, based on a previous report [13]. If the standard normal deviate was 1.96 [with a 95% confidence interval (CI)], the width of the CI being ±0.10, the required sample size of individuals with malnutrition was 196. Based on our previous study, the expected prevalence of malnutrition was 42% [3]. Hence, we set a duration of 2 years to retrospectively collect the data of 467 participants.

Statistical analysis

All statistical analyses were performed using SPSS, version 21 (IBM Corp., Armonk, NY, USA). The parametric data were expressed as the mean (SD), whereas nonparametric data were presented as the median and interquartile range (IQR). We compared the basic characteristics and outcome measures between the two groups using the unpaired *t*-test, the chi-squared test, Fisher's exact test, the Mann–Whitney *U*-test and the Kruskal–Wallis test, followed by Bonferroni correction or Dunn's test for multiple comparisons (>2 groups) [35]. In addition, we performed linear regression analysis and binary logistic regression analysis to assess the impact of malnutrition on the outcome variables [35]. Variables that exhibited a marked difference between the M and non-M groups in the univariate analysis were included in the multivariable analysis. $P < 0.05$ was considered statistically significant.

Results

Figure 1 outlines the flow diagram of the study participants and the categorisation of malnutrition using the ESPEN-DCM. During the study period, data from 520 patients were obtained. Of these, we excluded 26 patients with missing albumin data, two patients who were not clearly diagnosed with stroke and 72 patients with missing data for usual body weight. Finally, we enrolled 420 patients for the data analysis. Based on the ESPEN-DCM, 125 patients were assigned to the M group and 295 to the

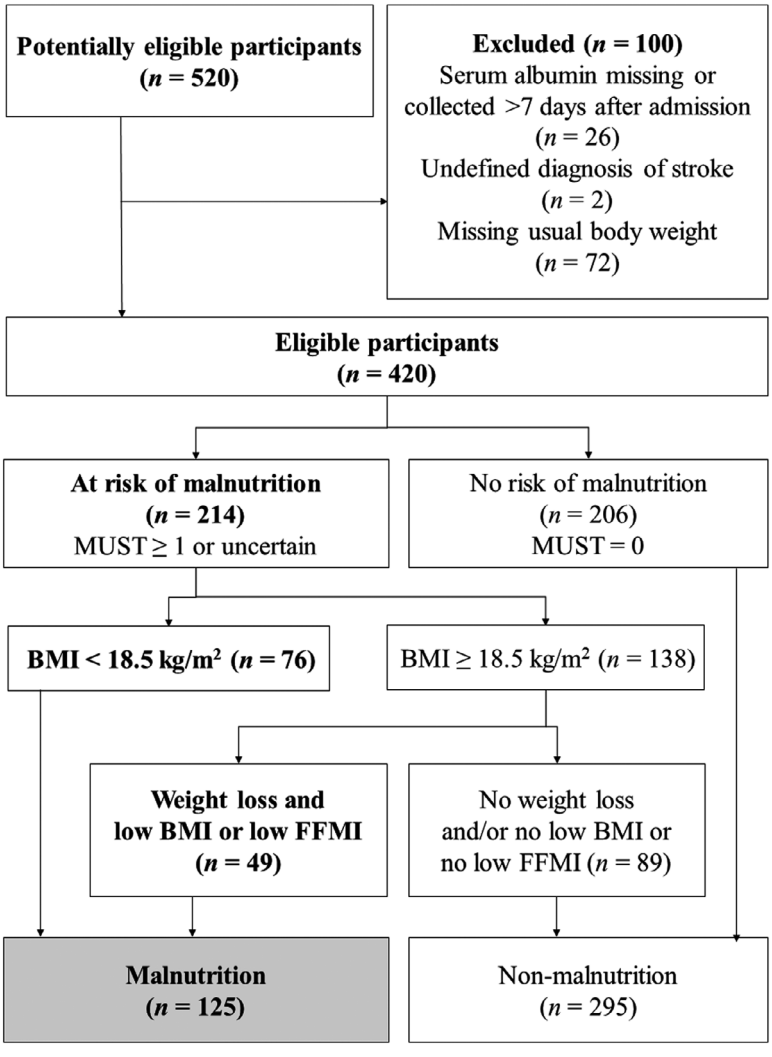

Figure 1 Flow diagram of study participants. MUST, Malnutrition Universal Screening Tool; BMI, body mass index; FFMI, fat-free mass index. Weight loss: >5% per 3 months or >10% indefinite of time. Low BMI: <20 kg m^{-2} for individuals aged <70 years or <22 kg m^{-2} for those aged ≥70 years. Low FFMI: <15 kg m^{-2} for females; <17 kg m^{-2} for males.

non-M group. Compared with the excluded patients, the patients included in the analysis had greater FIM (median 70 versus 57.5; $P = 0.004$), as well as higher MNA-SF (median 7 versus 5.5; $P = 0.003$) and GNRI scores (median 95.3 versus 92.8; $P = 0.014$).

Table 1 presents the demographic data of the enrolled patients. Compared with the non-M group, the patients in the M group were older, had a higher proportion of females, subarachnoid haemorrhage, dysphagia and certification of LTCI. In addition, the M group exhibited longer onset-admission duration, lower frequencies of cerebral infarction and dyslipidaemia, and lower FIM compared to those in the non-M group. The receiver-operating characteristics curves suggested that the areas under the curve for both the MNA-SF and GNRI were 0.890 and 0.865, respectively (Fig. 2). Based on the Youden index, the MNA-SF scores of 5 points (Se: 0.784; Sp: 0.847) and 7 points (Se: 0.960; Sp: 0.570) were optimal for detecting malnutrition and identifying the risk of malnutrition, respectively. Conversely, the well-established cut-off value for 'at risk of malnutrition' (≤11 points) revealed a markedly low Sp (0.017) (Table 2). Furthermore, the optimal cut-off values of the GNRI for detecting malnutrition were 92 (Se: 0.744; Sp: 0.841) and 98 (Se: 0.928; Sp: 0.502), which were the same as the well-established cut-off values for severe/moderate and mild malnutrition risk, respectively.

At discharge, the M group exhibited a lower FIM (median: 80 versus 114; $P < 0.001$), a higher frequency of discharge to acute care hospitals (26% versus 14%; $P < 0.001$) and fewer individuals returning home (49% versus 77%; $P < 0.001$). Likewise, individuals with a lower MNA-SF score (both 0–5 and 6–7) and GNRI (both <92 and 92–<98) exhibited a significantly lower FIM and were less likely to return home than those with higher scores based on the univariate analysis (Table 3).

Table 1 Demographic characteristics of 420 elderly patients with stroke in the convalescent rehabilitation wards

	Overall	M	Non-M	*P*
Number of subjects	420	125	295	
Age (years), mean (SD)	78.1 (7.9)	80.1 (8.0)	77.2 (7.6)	<0.001‡
Female, *n* (%)	171 (40.7)	61 (48.8)	110 (37.3)	0.028§
Onset-admission duration (days)				
median (IQR)	24 (18–34)	28 (20–40.5)	23 (17–32)	<0.001¶
Stroke subtype, *n* (%)				
Cerebral infarction	296 (70.5)	78 (62.4)*	218 (73.9)*	0.019§
Intracerebral haemorrhage	105 (25.0)	37 (29.6)	68 (23.1)	
Subarachnoid haemorrhage	19 (4.5)	10 (8.0)*	9 (3.1)*	
Stroke region, *n* (%)				
Supratentorial	321 (76.4)	95 (76.0)	226 (76.6)	0.095§
Infratentorial	39 (9.3)	8 (6.4)	31 (10.5)	
Both	41 (9.8)	12 (9.6)	29 (9.8)	
Not classifiable	19 (4.5)	10 (8.0)	9 (3.1)	
Paralysis, *n* (%)				
Hemiplegia	316 (75.2)	99 (79.2)	217 (73.6)	0.173§
Tetraplegia	18 (4.3)	7 (5.6)	11 (3.7)	
Absence	86 (20.5)	19 (15.2)	67 (22.7)	
Disabilities, *n* (%)				
Dysphagia	162 (38.6)	76 (60.8)	86 (29.2)	<0.001§
Aphasia	94 (22.4)	34 (27.2)	60 (20.3)	0.123§
Dysarthria	94 (22.4)	46 (36.8)	124 (42.0)	0.318§
Comorbidities, *n* (%)				
Diabetes mellitus	104 (24.8)	26 (20.8)	78 (26.4)	0.221§
Dyslipidaemia	151 (36.0)	25 (20.0)	126 (42.7)	<0.001§
Hypertension	347 (82.6)	98 (78.4)	249 (84.4)	0.137§
Artificial fibrillation	130 (31.0)	39 (31.2)	91 (30.8)	0.943§
Chronic kidney disease	48 (11.4)	9 (7.2)	39 (13.2)	0.076§
Recurrent stroke, *n* (%)	113 (26.9)	31 (24.8)	82 (27.8)	0.527§
Pre-stroke ADL, dependent, *n* (%)†	82 (19.5)	33 (26.4)	49 (16.6)	0.021§
Total FIM, median (IQR)	70 (40.3–93)	45 (25–75)	79 (54–101)	<0.001¶
BMI (kg m^{-2}), mean (SD)	22.1 (3.6)	18.2 (2.1)	24.0 (2.6)	<0.001‡
eFFMI (kg m^{-2}), median (IQR)	16.6 (14.7–18.3)	14.9 (12.3–16.3)	17.6 (15.4–18.8)	<0.001¶

ADL, activities of daily living; BMI, body mass index; eFFMI, estimated fat-free mass index; FIM, the Functional Independence Measure; IQR, interquartile range; M, malnutrition group; non-M, non-malnutrition group.

*$P < 0.05$ for other group by Bonferroni correction.

†Defined by the pre-stroke certification for the public long-term care insurance 'care level 1' or more.

‡Unpaired *t*-test.

§Chi-square test.

¶Mann–Whitney *U*-test.

After adjustment for covariates by multivariate analysis, a GNRI score of <92 remained significant for the prediction of risk for transfer to an acute care hospital [odds ratio (OR) = 3.12; 95% CI = 1.09–8.92]. However, no relationship was observed between the GNRI score of 92–<98, the MNA-SF (both 0–5 and 5–7) or ESPEN-DCM and the outcome measures (Table 4). In addition, we saw differences in the predictive capacity between the two criteria used in the ESPEN-DCM for outcome measures. Malnutrition defined by BMI <18.5 kg m^{-2} predicted a low FIM at discharge (B: −4.85; 95% CI = −9.61 to −0.08), a high tendency for transfer to an acute care hospital (OR = 2.76; 95% CI = 1.29–5.89) and a low possibility for returning home (OR = 0.30; 95% CI = 0.15–0.58). Such predictive capacity was not seen when malnutrition was defined by weight loss and low BMI (<20 kg m^{-2} for individuals aged <70 years or <22 kg m^{-2} for those aged ≥70 years) or low FFMI (<15 kg m^{-2} for females; <17 kg m^{-2} for males).

Discussion

The present study reports several clinical findings. First, when cut-off values of 5 and 7 points were applied, the MNA-SF exhibited a fair concurrent validity for malnutrition in patients with stroke in convalescent rehabilitation

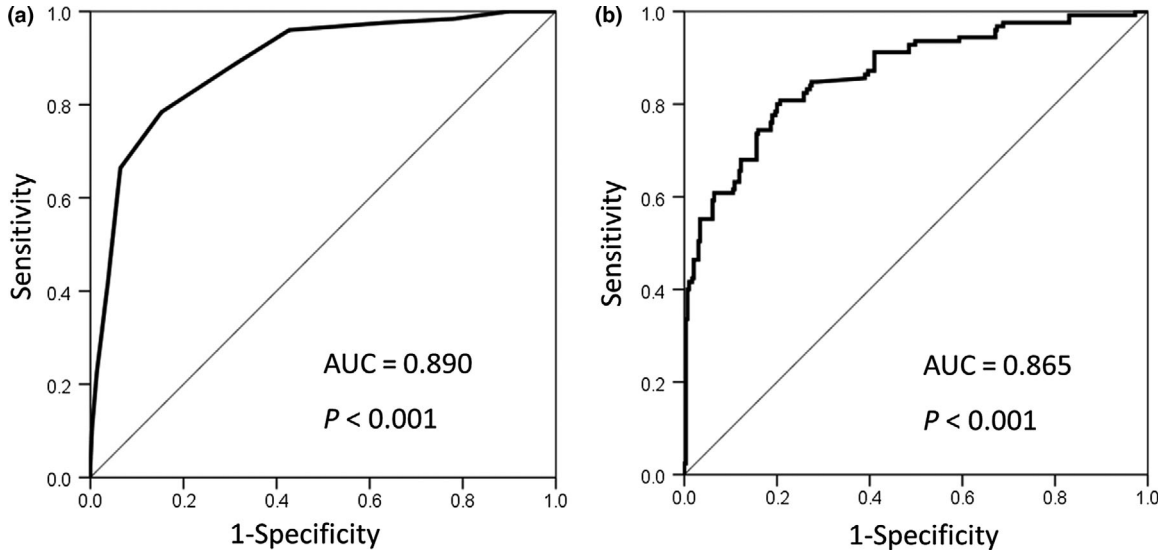

Figure 2 The receiver-operating characteristics curve of two malnutrition screening tools for malnutrition based on the reference standard. AUC, area under the curve. (a) Mini Nutritional Assessment Short-Form (MNA-SF). (b) Geriatric Nutritional Risk Index (GNRI).

Table 2 The accuracy of the Mini Nutritional Assessment Short-Form (MNA-SF) and Geriatric Nutritional Risk Index (GNRI) using various cut-off values against the diagnostic criteria for malnutrition

	Se	Sp	Kappa	The Youden index [31]
MNA-SF				
≤5*	0.784	0.847	0.606	0.631
≤7†	0.960	0.573	0.417	0.533
≤11	1.000	0.017	0.010	0.017
GNRI				
<92*	0.744	0.841	0.559	0.585
<98†	0.928	0.502	0.323	0.430

Se, sensitivity; Sp, specificity.
*Optimal cut-off value for identifying malnutrition determined by the Youden index.
†Optimal cut-off value for malnutrition screening determined by Se >90% and Sp >50%.

wards. Second, the GNRI also exhibited a fair concurrent validity with its established cut-off values. Third, the GNRI had good predictive validity for transferring to acute care hospital, whereas the MNA-SF did not show predictive capacity for any outcomes after multivariable analysis.

In the present study, the MNA-SF exhibited a high accuracy in determining malnutrition as defined by the ESPEN-DCM; however, the appropriate cut-off values (5 or 7 points) were far from its well-established values (7 or 11 points). Originally, cut-off values for the MNA-SF (7 and 11 points) were established based on agreement with the MNA [13]. However, this approach may involve the risk of incorporation bias because the MNA-SF was initially derived from the components of the MNA. The present study has strength regarding methodology because the validity of the MNA-SF was assessed against the ESPEN-DCM with the MUST to avoid incorporation bias. A previous study reported that the MNA-SF might pose a risk of overestimation of malnutrition when using a cut-off value of 11 points because of markedly low specificity in older adults in a rehabilitation unit [15] or a geriatric care hospital [36]. Similarly, we previously reported that 99% of convalescent stroke patients were assessed as 'at risk of malnutrition' if a score of 11 points in the MNA-SF was used for malnutrition screening [3]. The lower cut-off score of the MNA-SF might be appropriate for patients with stroke because some of the subscoring categories of this tool, such as mobility or neuropsychological problems, could also be diminished by stroke sequela *per se* (i.e. hemiparesis or aphasia). From the perspective of clinical practice, we recommend that older adults after stroke can be identified as at risk of malnutrition with a score of ≤7 points on the MNA-SF during the rehabilitation period whereas those with malnutrition can be identified by a score of ≤5 points. On the other hand, the accuracy of a malnutrition screening tool depends on whether the components of the tool can appropriately represent and address the characteristic features of malnutrition. The MNA-SF (revised version) has not been investigated in terms of its construct and content validities; however, it is likely to have content validity because the original MNA-SF had ensured construct validity [37]. Whether its components are valid for an individual with disabilities is a question that remains to be evaluated.

The present study demonstrated that the GNRI with the established criteria (92 and 98 points) is useful for detecting

Table 3 The predictive capacity of the Mini Nutritional Assessment Short-Form (MNA-SF) and Geriatric Nutritional Risk Index (GNRI) based on the new cut-off value

	MNA-SF			GNRI		
	0–5	6–7	8–14	<92	92 to <98	>98
Number of subjects	143	103	174	139	124	157
Discharge FIM, median (IQR)	71 (36–105)*	105 (69–119)*	119.5 (109.8–123)*	71 (35–102)*	109 (79.3–120)*	120 (110.5–123)*
Discharge destination, *n* (%)						
Home	66 (46.1)†	71 (68.9)†	152 (87.4)†	62 (44.6)†	91 (73.4)†	136 (86.6)†
Long-term care	40 (28.0)†	13 (12.6)†	6 (3.4)†	34 (24.5)†	15 (12.1)	10 (6.4)
Acute care hospital	37 (25.9)‡	19 (18.4)	16 (9.2)	43 (30.9)†	18 (14.5)	11 (7.0)

FIM, Functional Independence Measure; IQR, interquartile range; MNA-SF.

*$P < 0.001$ for other groups by Kruskal–Wallis test and Dunn's test.

†$P < 0.05$ for other groups by chi-squared test and Bonferroni correction.

‡$P < 0.05$ for the group with a score of 8–14 by the chi-squared test and Bonferroni correction.

and screening for malnutrition in older patients with stroke in the rehabilitation phase. Initially, the GNRI was developed as an indicator of nutritional risk [16]. The cut-off values of 92 and 98 were initially established from the hypothetical combination of albumin and weight-to-ideal-body-weight ratio and assessed predictive ability against mortality and the risk of complications [16]. However, it cannot be assumed that it is accurate indicator of nutritional status [16,19] because of its dependence on objective biomarkers and low accuracy with respect to detecting the reference standard of malnutrition [19]. The reason the GNRI exhibited fair concurrent validity in the present study is unclear, although characteristics of malnutrition in stroke survivors and timing of the nutritional assessment may partially explain this inconsistency. Because malnutrition in patients with stroke is primarily caused by dysphagia [1], it is classified as 'disease-related malnutrition without inflammation' [38]. In addition, the present study only enrolled patients with stroke in the rehabilitation phase. Thus, the effect of factors affecting albumin (i.e. components of the GNRI), such as inflammation and disease stress, in this population might be weaker than in acute or inflammatory diseases. Albumin does not indicate nutritional status but instead inflammatory status [39]. Therefore, it is possible that the patients screened by the GNRI have either inflammatory disease or malnutrition. From this standpoint, we recommend the use of MNA-SF for patients after stroke. However, if MNA-SF cannot be used for certain patients, the use of GNRI may be acceptable if accompanied by assessment of hydration and inflammatory status, as well as the presence of diseases that cause hypoalbuminaemia. The validity of the GNRI is unclear when the BMI is applied to ideal body weight. However, GNRI based on a BMI of 22 kg m^{-2} showed a linear correlation with those based on the Lorentz formula in Japanese patients [29]. Therefore, we consider that our results are valid even when BMI is used in calculation of the GNRI.

The present study also indicated the predictive validity of the GNRI against transfer to acute care hospital, whereas the same was not observed with the use of the MNA-SF. Only one ESPEN-DCM criterion (BMI <18.5 kg m^{-2}) was an independent predictor of discharge FIM and return home, whereas other criteria (weight loss and low BMI or FFMI) did not predict these outcomes. Patients with stroke often experience a reduction in their body weight, approximately 3 kg in the acute phase, particularly in those whose body weight is higher than the normal [40]. A decreased body weight could be attributed to muscle atrophy that is primarily caused in paretic limbs [41] and the diminished nutritional intake because of dysphagia [42]. Thus, it could be hypothesised that a combination of the loss of body weight during the acute phase and the current BMI or FFMI reflect not only nutritional status, but also the severity of hemiparesis or a loss of body weight in overweight/obese patients. Conversely, malnourished status at the time of onset or stroke can predict clinical outcomes [4,5]. Individuals with BMI <18.5 kg m^{-2} in the present study may include patients who had developed malnutrition before the onset of stroke; thus, the ESPEN-DCM based on low BMI solely exerted more impact on rehabilitation outcomes. Many previous studies employed length of hospital stay, mortality and complication rates as outcomes of predictive validity; fewer studies used functional outcomes and discharge destination [25]. Although we consider that the latter outcomes may be preferred to the former for predictive validity during inpatient rehabilitation, further research is required to determine the appropriate outcomes for validity of malnutrition screening tools in the rehabilitation setting.

The concurrent validity of the MNA-SF and the GNRI needs to be re-evaluated under the international diagnostic criteria for malnutrition (Global Leadership Initiative on Malnutrition: GLIM criteria). The four scientific societies for clinical nutrition endorsed the GLIM criteria in

Table 4 The multivariable analysis for the various outcome measures using the European Society for Clinical Nutrition and Metabolism diagnostic criteria for malnutrition (ESPEN-DCM), Mini Nutritional Assessment Short-Form (MNA-SF) and Geriatric Nutritional Risk Index (GNRI)

	ESPEN-DCM			MNA-SF‡		GNRI§	
Outcome measures	Overall	Criterion 1†	Criterion 2†	0–5	6–7	<92	92 to <98
FIM at discharge (continuous)							
B (95% CI)¶	−2.20 (−6.22 to 1.81)	−4.85 (−9.61 to −0.08)*	2.12 (−3.19 to 7.43)	−0.48 (−5.57 to 4.61)	0.15 (−4.42 to 4.72)	−3.56 (−8.66 to 1.54)	2.11 (−2.26 to 6.47)
Discharge destination							
Home							
OR (95% CI)¶	0.63 (0.37–1.09)	0.30 (0.15–0.58)*	2.12 (0.98–4.60)	0.68 (0.33–1.40)	0.80 (0.40–1.63)	0.59 (0.29–1.22)	0.92 (0.46–1.87)
Long-term care							
OR (95% CI)¶	1.58 (0.81–3.08)	1.39 (0.67–2.88)	1.41 (0.59–3.39)	2.04 (0.69–6.04)	1.47 (0.49–4.42)	0.80 (0.30–2.12)	0.86 (0.33–2.28)
Acute care							
OR (95% CI)¶	1.46 (0.73–2.93)	2.76 (1.29–5.89)*	0.37 (0.11–1.28)	1.16 (0.44–3.05)	1.48 (0.59–3.70)	3.12 (1.09–8.92)*	1.89 (0.69–5.14)

B, partial regression coefficient; CI, confidence interval; FIM, Functional Independence Measure; OR, odds ratio.

*$P < 0.05$.

†Alternative ways for identifying malnutrition by the ESPEN-DCM: criterion 1, body mass index (BMI) < 18.5 kg m^{-2}; criterion 2, unintentional weight loss (>5% per 3 months or >10% for undefined time) and low BMI (<20 kg m^{-2} for individuals aged <70 years or <22 kg m^{-2} for those aged ≥70 years) or low fat-free mass index (<15 kg m^{-2} for females or <17 kg m^{-2} for males).

‡Reference value: 8–14 points.

§Reference value: ≥98.

¶Adjusted for age, sex, onset-admission duration, stroke type (reference: cerebral infarction) dysphagia, dyslipidaemia, prestroke activities of daily living and FIM at admission.

2018 [38]. The phenotypic criteria in the GLIM criteria (loss of body weight, low BMI and low muscle mass) are similar to the ESPEN-DCM. However, the aetiology of malnutrition, which is a necessary component of the GLIM criteria, is not taken into account in the ESPEN-DCM. Therefore, some patients who were diagnosed as malnourished by the ESPEN-DCM might not be malnourished when the GLIM criteria are applied. In addition, the present study investigated only Asian patients. Because the cut-off value of BMI for malnutrition in the Asian population is different from that in the Western population [38], the cut-off values of the MNA-SF and the GNRI established in the present study will require further evaluation to apply to a wider population.

The present study had several limitations. First, we did not acquire the measured FFMI using bioimpedance analysis or dual-energy X-ray absorptiometry because of the retrospective nature of the study. Instead, we substituted eFFMI for measured FFMI. Second, we could not adjust all potential confounders, such as the severity of stroke, in the multivariate analysis because these were not included in the original dataset. However, we used the FIM at admission, which correlates with the stroke severity [43]. Third, the present study excluded the patients who could not be diagnosed with malnutrition as a result of a lack of information regarding their usual body weight. Because the excluded patients showed a lower MNA-SF and GNRI score, the prevalence of malnutrition might be underestimated. Whether this limitation could lead to a bias in the accuracy of the MNA-SF and the GNRI against the reference standard remains unclear, although future studies employing malnutrition screening tool(s) that do not require usual body weight will be required. Fourth, because the present study included only the Asian population, the cut-off values might not be appropriate for a non-Asian population. Lastly, our findings may need to be re-evaluated under the GLIM criteria for malnutrition diagnosis.

In conclusion, the MNA-SF (using 5 and 7 points for detecting malnutrition and malnutrition screening, respectively) and GNRI (using a score of 92 and 98, respectively) exhibit fair concurrent validity against the ESPEN-DCM in older patients with stroke during the rehabilitation phase. Although the GNRI indicated predictive validity for transferring to an acute care hospital, the MNA-SF did not predict any outcomes of inpatient rehabilitation. The findings of the present study can be generalised to all patients with stroke in the sub-acute or rehabilitation setting; however, whether these can be applied to patients with acute stroke or to non-Asian patients remains unclear. Hence, further studies are warranted to verify the appropriateness of the cut-off value of the MNA-SF and GNRI derived from our study for a diverse group of patients.

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Conflict of interests, source of funding and authorship

The authors declare that they have no conflicts of interest.
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SN was responsible for the conception and design of the study, acquisition of data, analysis and interpretation of data, and drafting of the paper. KO, JK and YT were responsible for the analysis and interpretation of data and revising the paper critically for important intellectual content. EN and NM were responsible for the conception and design of the study, acquisition of data, and revising the paper critically for important intellectual content. All authors critically reviewed the manuscript and approved the final version submitted for publication.

Transparency declaration

The lead author affirms that this manuscript is an honest, accurate and transparent account of the study being reported. The reporting of this work is compliant with STARD guidelines.

References

1. Foley NC, Salter KL, Robertson J *et al.* (2009) Which reported estimate of the prevalence of malnutrition after stroke is valid? *Stroke* **40**, e66–e74.
2. Kaiser MJ, Bauer JM, Rämsch C *et al.* (2010) Frequency of malnutrition in older adults: a multinational perspective using the mini nutritional assessment. *J Am Geriatr Soc* **58**, 1734–1738.
3. Nishioka S, Wakabayashi H & Yoshida T (2017) Accuracy of non-paralytic anthropometric data for nutritional screening in older patients with stroke and hemiplegia. *Eur J Clin Nutr* **71**, 173–179.
4. The FOOD Trial Collaboration (2003) Poor nutritional status on admission predicts poor outcomes after stroke: observational data from the FOOD trial. *Stroke* **34**, 1450–1456.
5. Gomes F, Emery PW & Weekes CE (2016) Risk of malnutrition is an independent predictor of mortality, length of hospital stay, and hospitalization costs in stroke patients. *J Stroke Cerebrovasc Dis* **25**, 799–806.
6. Nishioka S, Okamoto T, Takayama M *et al.* (2017) Malnutrition risk predicts recovery of full oral intake among older adult stroke patients undergoing enteral nutrition: secondary analysis of a multicentre survey (the APPLE study). *Clin Nutr* **36**, 1089–1096.
7. Nii M, Maeda K, Wakabayashi H *et al.* (2016) Nutritional improvement and energy intake are associated with functional recovery in patients after cerebrovascular disorders. *J Stroke Cerebrovasc Dis* **25**, 57–62.
8. Nishioka S, Wakabayashi H, Nishioka E *et al.* (2016) Nutritional improvement correlates with recovery of activities of daily living among malnourished elderly stroke patients in the convalescent stage: a cross-sectional study. *J Acad Nutr Diet* **116**, 837–843.
9. Malnutrition Action Group (MAG) (a standing committee of the British Association for Parenteral and Enteral Nutrition). The "MUST" explanatory booklet. http://www.bapen.org.uk/pdfs/must/must_explan.pdf (accessed 15 November 2018).
10. Burgos R, Bretón I, Cereda E *et al.* (2018) ESPEN guideline clinical nutrition in neurology. *Clin Nutr* **37**, 354–396.
11. Cederholm T, Bosaeus I, Barazzoni R *et al.* (2015) Diagnostic criteria for malnutrition – An ESPEN consensus statement. *Clin Nutr* **34**, 335–340.
12. Poulia KA, Klek S, Doundoulakis I *et al.* (2017) The two most popular malnutrition screening tools in the light of the new ESPEN consensus definition of the diagnostic criteria for malnutrition. *Clin Nutr* **36**, 1130–1135.
13. Kaiser M, Bauer J, Ramsch C *et al.* (2009) Validation of the mini nutritional assessment short-form (MNA®-SF); a practical tool for identification of nutritional status. *J Nutr Health Aging* **13**, 782–788.
14. Kondrup J, Allison SP, Elia M *et al.* (2003) ESPEN guidelines for nutrition screening 2002. *Clin Nutr* **22**, 415–421.
15. Marshall S, Young A, Bauer J *et al.* (2016) Nutrition screening in geriatric rehabilitation: criterion (concurrent and predictive) validity of the Malnutrition Screening Tool and the Mini Nutritional Assessment–Short Form. *J Acad Nutr Diet* **116**, 795–801.
16. Bouillanne O, Morineau G, Dupont C *et al.* (2005) Geriatric Nutritional Risk Index: a new index for evaluating at-risk elderly medical patients. *Am J Clin Nutr* **82**, 777–783.
17. Kokura Y, Maeda K, Wakabayashi H *et al.* (2016) High nutritional-related risk on admission predicts less improvement of Functional Independence Measure in geriatric stroke patients: a retrospective cohort study. *J Stroke Cerebrovasc Dis* **25**, 1335–1341.
18. Maruyama K, Nakagawa N, Koyama S *et al.* (2018) Malnutrition increases the incidence of death, cardiovascular events, and infections in patients with stroke after rehabilitation. *J Stroke Cerebrovasc Dis* **27**, 716–723.
19. Cereda E, Pusani C, Limonta D *et al.* (2009) The ability of the Geriatric Nutritional Risk Index to assess the nutritional status and predict the outcome of home-care

resident elderly: a comparison with the Mini Nutritional Assessment. *Br J Nutr* **102**, 563–570.
20. Miyai I, Sonoda S, Nagai S *et al.* (2011) Results of new policies for inpatient rehabilitation coverage in Japan. *Neurorehabil Neural Repair* **25**, 540–547.
21. Tamiya N, Noguchi H, Nishi A *et al.* (2011) Population ageing and wellbeing: lessons from Japan's long-term care insurance policy. *Lancet* **378**, 1183–1192.
22. Miyazawa Y, Chikamori M, Uchiyama S *et al.* (2005) The Knee-Height method and its challenge. *Rinsho Eiyo* **107**, 411–416 (article in Japanese).
23. Elia M & Stratton RJ (2011) Considerations for screening tool selection and role of predictive and concurrent validity. *Curr Opin Clin Nutr Metab Care* **14**, 425–433.
24. Youden WJ (1950) Index for rating diagnostic tests. *Cancer* **3**, 32–35.
25. van Bokhorst-de van der Schueren MAE, Guaitoli PR, Jansma EP *et al.* (2014) Nutrition screening tools: does one size fit all? A systematic review of screening tools for the hospital setting. *Clin Nutr* **33**, 39–58.
26. Chumney D, Nollinger K, Shesko K *et al.* (2010) Ability of Functional Independence Measure to accurately predict functional outcome of stroke-specific population: systematic review. *J Rehabil Res Dev* **47**, 17–29.
27. Kaiser R, Winning K, Uter W *et al.* (2009) Comparison of two different approaches for the application of the Mini Nutritional Assessment in nursing homes. *J Nutr Health Aging* **13**, 863–869.
28. Buzby GP, Knox LS, Crosby L *et al.* (1988) Study protocol: a randomized clinical trial of total nutrition in malnourished. *Am J Clin Nutr* **47**, 366–381.
29. Yamada K, Furuya R, Takita T *et al.* (2008) Simplified nutritional screening tools for patients on maintenance hemodialysis. *Am J Clin Nutr* **87**, 106–113.
30. Cereda E, Pedrolli C, Zagami A *et al.* (2011) Nutritional screening and mortality in newly institutionalised elderly: a comparison between the geriatric nutritional risk index and the mini nutritional assessment. *Clin Nutr* **30**, 793–798.
31. Rondel AL, Langius JA, de van der Schueren MA *et al.* (2018) The new ESPEN diagnostic criteria for malnutrition predict overall survival in hospitalised patients. *Clin Nutr* **37**, 163–168.
32. Sánchez-Rodríguez D, Marco E, Ronquillo-Moreno N *et al.* (2017) Prevalence of malnutrition and sarcopenia in a post-acute care geriatric unit: applying the new ESPEN definition and EWGSOP criteria. *Clin Nutr* **36**, 1339–1344.
33. Jassal SK, Wassel CL, Laughlin GA *et al.* (2015) Urine creatinine-based estimates of fat-free mass in community-dwelling older persons: the Rancho Bernardo study. *J Ren Nutr* **25**, 97–102.
34. Ix JH, Wassel CL, Stevens LA *et al.* (2011) Equations to estimate creatinine excretion rate: the CKD epidemiology collaboration. *Clin J Am Soc Nephrol* **6**, 184–191.
35. Woolson RF & Clarke WR (2002) *Statistical Methods for the Analysis of Biomedical Data*, 2nd edn. New York, NY: John Wiley & Sons. Inc.
36. Baek MH & Heo YR (2015) Evaluation of the efficacy of nutritional screening tools to predict malnutrition in the elderly at a geriatric care hospital. *Nutr Res Pract* **9**, 637–643.
37. Power L, Mullally D, Gibney ER *et al.* (2018) A review of the validity of malnutrition screening tools used in older adults in community and healthcare settings – A MaNuEL study. *Clin Nutr ESPEN* **24**, 1–13.
38. Cederholm T, Barazzoni R, Austin P *et al.* (2017) ESPEN guidelines on definitions and terminology of clinical nutrition. *Clin Nutr* **36**, 49–64.
39. Cederholm T, Jensen GL, Correia MITD *et al.* (2019) GLIM criteria for the diagnosis of malnutrition – A consensus report from the global clinical nutrition community. *Clin Nutr* **38**, 1–9.
40. Paquereau J, Allart E, Romon M *et al.* (2014) The long-term nutritional status in stroke patients and its predictive factors. *J Stroke Cerebrovasc Dis* **23**, 1628–1633.
41. English C, McLennan H, Thoirs K *et al.* (2010) Loss of skeletal muscle mass after stroke: a systematic review. *Int J Stroke* **5**, 395–402.
42. Foley NC, Martin RE, Salter KL *et al.* (2009) A review of the relationship between dysphagia and malnutrition following stroke. *J Rehabil Med* **41**, 707–713.
43. Roth EJ, Heinemann AW, Lovell LL *et al.* (1998) Impairment and disability: their relation during stroke rehabilitation. *Arch Phys Med Rehabil* **79**, 329–335.

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OLDER ADULTS

Are hypohydrated older adults at increased risk of exhaustion?

I. Anjo,[1] T. F. Amaral,[1,2] C. Afonso,[1,3] N. Borges,[1,4] A. Santos,[1,5] P. Moreira[1,3,6] & P. Padrão[1,3]

[1]Faculdade de Ciências da Nutrição e Alimentação da, Universidade do Porto, Porto, Portugal
[2]Faculdade de Engenharia, UISPA-IDMEC, Universidade do Porto, Porto, Portugal
[3]EPIUnit – Instituto de Saúde Pública, Universidade do Porto, Porto, Portugal
[4]CINTESIS – Centre for Health Technology and Services Research, Porto, Portugal
[5]I3S-Instituto de Investigação e Inovação em Saúde, Porto, Portugal
[6]Centro de Atividade Física, Saúde e Lazer, Universidade do Porto, Porto, Portugal

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Correspondence
P. Padrão, Faculty of Nutrition and Food Sciences, University of Porto, Rua Doutor Roberto Frias, 4200-465 Porto, Portugal.
Tel.: +351 22 5074320
Fax: +351 22 5074329
E-mail: patriciapadrao@fcna.up.pt

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Abstract

Background: Dehydration appears to affect muscle strength and weakness, although its influence on exhaustion remains unclear. The present study aimed to quantify the association between hydration status and exhaustion among older adults.
Methods: A cluster sampling approach was used, representing Portuguese older adults (≥65 years) according to age, sex, education level and region within the Nutrition UP65 cross-sectional study. A 24-h urine sample was collected to estimate free water reserve (FWR), which was categorised into tertiles according to sex. Subjects with incomplete 24-h urine and renal disease were excluded. From a sample size of 1500 subjects, 1143 were eligible. Exhaustion was self-reported according to the Center for Epidemiologic Studies Depression Scale. A logistic regression model was conducted to evaluate the association between FWR and exhaustion. Odds ratios and the respective 95% confidence intervals were calculated by sex and age.
Results: Free water reserve median (interquartile range) was 0.52 (0.68) L in women and 0.36 (0.77) L in men. Hypohydration affected 11.6% of women and 25.1% of men, whereas exhaustion was reported by 39.3% of women and 25.1% of men. After adjusting for confounders, women ≥80 years classified in the highest tertile of FWR showed a decreased risk of exhaustion (third tertile: odds ratio = 0.38; 95% confidence interval = 0.15–0.96) compared to women in the lowest FWR tertile. No such significant association was observed in women with <80 years and in men.
Conclusions: These results show an association between worse hydration status and exhaustion in older women, highlighting the need to implement further studies clarifying this association.

Introduction

Water is an essential nutrient for all functions of the human body, representing 50–60% of total body mass [(1,2)]. Along with other functions, water supports cellular homeostasis, transports nutrients and is a crucial component of thermoregulation [(3)]. There are large differences in the fluid intake and losses of individuals and so the hydration status is not uniform across populations [(4)]. Water requirement depends on several factors, such as renal solute load, climate and physical activity, and a low intake of total water has been associated with a number of negative effects on health [(1)]. Dehydration, which is 'the process of losing water and leading eventually to hypohydration (the condition of body water deficit)' [(5,6)], and even to mild dehydration, which is defined as a 1–

2% loss in body mass caused by fluid loss, affects overall health and increases various morbidities [1,7].

The adequate total water intake for men is estimated to be 2.5 L day^{-1} and 2.0 L day^{-1} for women [6] although the daily water supply of the older population is frequently lower than the recommended [8]. Older persons have a deficit in thirst and regulation of fluid intake – the thirst response is less effective as a result of changes in the activity of osmoreceptors and, consequently, a decrease in fluid intake [3,6]. Also, the loss of fluid may not be as well controlled, the fluid reserve is smaller and the kidney functions decline, such that the ability to concentrate urine and retain fluids falls [5,9]. Furthermore, the hydration risk can be exacerbated by the use of diuretics and a wide range of medications, commonly used by older people [10]. These changes lead to an increased risk of hypohydration and some of the symptoms are connected to impaired functional status, physical performance and the development of several diseases [1,11].

Muscle performance declines with ageing and a hypohydrated status appears to lead to a decrease in muscle strength [12] although how hydration status impacts exhaustion and wellness remains unclear [10]. Therefore, the present study aimed to quantify the association between hydration status and perceived exhaustion among older adults.

Materials and methods

Study design and sampling

This cross-sectional observational study was conducted in a sample of 1500 Portuguese subjects ≥65 years old between December 2015 and June 2016, according to 'The Nutrition UP 65 Study Protocol' [13].

A nationally representative sample of Portuguese older adults was achieved in terms of sex, age, education level and regional area defined in the Nomenclature of Territorial Units for Statistical Purposes (NUTS II) [13]. The study sample comprised community-dwelling older adults (95%) and individuals institutionalised in retirement homes (5%) [13].

A random, stratified and clustered sampling method was applied. The potential participants were contacted by telephone, home approach or via institutions from interviewers who provided information about the study and invited them to participate. Individuals were considered eligible to participate if they had Portuguese nationality and if they were aged ≥65 years. Exclusion criteria were having any condition that precluded the collection of urine (e.g. dementia or urinary incontinence).

Data collection and variable definition

Sociodemographic and lifestyle characteristics, clinical history, nutritional status and physical activity were collected using a structured questionnaire applied by trained interviewers.

Sociodemographic data included information on sex, age and marital status. To analyse marital status, participants were grouped into two categories: single, divorced or widowed versus married or in a common-law marriage.

Lifestyle data included information on physical activity assessed by the short form of the International Physical Activity Questionnaire (IPAQ) [14]. Participants were classified as either presenting low physical activity levels [<383 kcal $week^{-1}$ (men) and <270 kcal $week^{-1}$ (women)] or normal physical activity levels [≥383 kcal $week^{-1}$ (men) and ≥270 kcal $week^{-1}$ (women)] [14].

Clinical data included medication and supplements assessed by self-reporting. Subjects with renal disease were excluded. The health status was also self-reported and classified by participants as very good, good, moderate bad or very bad.

Body weight and standing height were assessed and body mass index was computed using the standard formula [body weight (kg)/standing $height^2$ (m)]. World Health Organization cut-offs were used to define underweight (<18.5 kg m^{-2}), normal weight (18.5–24.9 kg m^{-2}), overweight (25.0–29.9 kg m^{-2}) and obesity (≥30.0 kg m^{-2}) [15]. Only two participants were classified as underweight and therefore underweight and normal weight participants were grouped into one category. Undernutrition was assessed by the Portuguese version of the Mini-Nutritional Assessment – Short-Form and participants were considered undernourished if the final score was ≤7 points and at risk of undernutrition if the final score was between 8 and 11 points. Participants with a score ≥12 points were classified without undernutrition risk/undernutrition [16].

Self-reported exhaustion was assessed using two items from the Center for Epidemiologic Studies Depression Scale [17]. The following two statements were read: (i) I felt that everything I did was an effort and (ii) I could not get going. Participants were asked 'How often in the last week did you feel this way?' and the response was classified as: 0 = rarely or none of the time (<1 day); 1 = some or little of the time (1–2 days); 2 = a moderate amount of the time (3–4 days); or 3 = most of the time (>4 days). The exhaustion criteria were considered present if the participant answered '2' or '3' to either of these questions [18]. According to Fried, self-reported exhaustion reflects poor endurance and energy. Self-reported exhaustion is associated with stage of exercise reached in graded exercise testing, as an indicator of VO_2 max, and is predictive of cardiovascular disease [18].

A 24-h urine sample was collected for each participant. The study interviewers gave the participants oral and written instructions detailing the collection and adequate

storage procedures for the 24-h urine volume. A leaflet was distributed to all participant/caregiver regarding how to proceed for a valid collection and adequate storage of the volume of 24-h urine. Participants/caregivers were taught to discard the first morning void and to collect all urine over the following 24 h, including the first void on the following morning, and to keep note of the time of the start and end of collection. A 24-h urine container (3 L) was also provided.

The following urinary markers were quantified by a certified laboratory: urine volume (mL), urinary creatinine (mg day^{-1}) and urine osmolality (mosmol kg^{-1}). Urinary creatinine was measured by the Jaffe method and osmolality was evaluated using an automatic osmometer. A urine sample was considered inadequate if the creatinine level was <0.4 g/24 h for women and <0.6 g/24 h for men or if the volume collected was <500 mL [19,20].

Hydration status was evaluated based on the concept of free water reserve (FWR) (mL/24 h) calculated by subtracting 24-h urine volume to obligatory urine volume [solutes in urine 24 h (mosmol day^{-1})/ 830 − 3.4 × (age − 20)] [1,21,22]. The participant was considered as euhydrated if FWR was positive or hypohydrated/at hypohydration risk if FWR was negative [22].

Statistical analysis

Categorical variables were reported as frequencies. FWR was described as the median and interquartile range (IQR). Participants were compared across tertiles of FWR and exhaustion status for several sociodemographic, lifestyle, clinical and nutritional characteristics using the Kruskal–Wallis test for continuous variables and the Pearson chi-squared test for categorical variables.

Binary logistic regression models were conducted to evaluate the association between perceived exhaustion and tertiles of FWR, adjusting for possible confounders. Odds ratio (OR) and respective 95% confidence intervals (95% CI) were calculated. $P < 0.05$ was considered statistically significant.

Statistical analyses were conducted using SPSS, version 24.0 (IBM Corp., Armonk, NY, USA).

Sensitivity analysis

We further tested the association between perceived exhaustion and tertiles of FWR excluding participants with self-reported chronic back pain ($n = 756$).

Ethical approval

The study protocol was approved by the Ethics Committee of the Department of Social Sciences and Health from the Faculty of Medicine of the University of Porto (no. PCEDCSS – FMUP 15/2015) and by the Portuguese National Commission of Data Protection (no. 9427/2015) and was conducted in accordance with the guidelines established by the Declaration of Helsinki. All participants were asked to read and sign a duplicated informed consent form.

Results

From the 1500 subjects recruited, 178 participants were excluded because urine samples were incomplete and 137 reported kidney disease, whereas 35 participants were excluded because they were not aware if they had that condition. Three participants did not complete the depression scale. For the other four participants, it was either not possible to measure or to estimate weight. Therefore, the final study sample comprised 1143 participants. A higher proportion of participants with inadequate 24-h urine collection among participants were living in retirement homes compared to those living in their own home (11.7% versus 3.9%, $P < 0.001$).

The characteristics of the 1143 subjects across tertiles of FWR and perceived exhaustion, according to sex are presented in Tables 1 and 2. Age ranged from 65 to 94 years with a median (IQR) equal to 73 (10.0) years and with women representing a higher proportion of the sample (55.7%).

FWR median (IQR) was 0.52 (0.68) L in women and 0.36 (0.77) L in men. The oldest women (≥85 years) presented a lower median FWR compared to women <80 years old (0.39 versus 0.54, $P = 0.015$), whereas no such difference was observed among men (0.43 versus 0.34, $P = 0.092$). Hypohydration affected 11.6% of women and 25.1% of men ($P < 0.001$). Exhaustion was reported by 39.3% of women and 25.1% of men ($P < 0.001$).

Higher proportions of women with normal physical activity, with a very good or good self-perception of health status and without exhaustion were found in the highest FWR tertile (Table 1). Most women aged 65–79 years, with normal physical activity, without undernutrition, with a very good/good self-perception of health status and included in the last FWR tertile did not report exhaustion (Table 1).

In men, higher proportions of participants married or in a common-law marriage, with normal physical activity, with an inadequate salt intake and without using diuretics were found in the first FWR tertile (Table 2). Most men with normal physical activity, without undernutrition and with a very good/good self-perception of health status did not report exhaustion (Table 2).

Significant differences according to physical activity and self-perception of health status were found between

Table 1 Sociodemographic, lifestyle, clinical, anthropometric and nutritional characteristics of 638 Portuguese older women (≥65 years old) according to FWR tertiles (L)

Participants' characteristics	First tertile, <0.306 L (*n* = 212)	Second tertile, 0.306–0.768 L (*n* = 214)	Third tertile, >0.768 L (*n* = 212)	*P*	With exhaustion (*n* = 251)	Without exhaustion (*n* = 387)	*P*
Age (years), *n* (%)							
65–79	153 (72.2)	159 (74.3)	171 (80.7)	0.105	169 (67.3)	314 (81.1)	<0.001
≥80	59 (27.8)	55 (25.7)	41 (19.3)		82 (32.7)	73 (18.9)	
Marital status, *n* (%)							
Single/divorced/widowed	127 (59.9)	129 (60.3)	132 (62.3)	0.867	163 (64.9)	225 (58.1)	0.097
Married/common-law marriage	85 (40.1)	85 (39.7)	80 (37.7)		88 (35.1)	162 (41.9)	
Physical activity (IPAQ) (kcal week^{-1}), *n* (%)							
Normal (men < 383; women < 270)	180 (84.9)	168 (78.5)	188 (88.7)	0.015	183 (72.9)	353 (91.2)	<0.001
Low (men ≥ 383; women ≥270)	32 (15.1)	46 (21.5)	24 (11.3)		68 (27.1)	34 (8.8)	
Body mass index, *n* (%)							
Underweight/normal	32 (15.1)	33 (15.4)	29 (13.7)	0.192	33 (13.1)	61 (15.8)	0.102
Overweight	80 (37.7)	88 (41.1)	104 (49.1)		98 (39.0)	174 (45.0)	
Obesity	100 (47.2)	93 (43.5)	79 (37.3)		120 (47.8)	152 (39.3)	
Nutritional status (MNA-SF), *n* (%)							
Without undernutrition	174 (82.1)	174 (81.3)	187 (88.2)	0.106	189 (75.3)	346 (89.4)	<0.001
With risk of undernutrition or undernourished	38 (17.9)	40 (18.7)	25 (11.8)		62 (24.7)	41 (10.6)	
Season urine sample collection, *n* (%)							
Autumn/winter	124 (58.5)	138 (64.5)	128 (60.4)	0.430	162 (64.5)	228 (58.9)	0.159
Spring/summer	88 (41.5)	76 (35.5)	84 (39.6)		89 (35.5)	159 (41.1)	
Salt intake (g), *n* (%)							
Adequate (<5)	49 (23.1)	38 (17.8)	46 (21.7)	0.370	56 (22.3)	77 (19.9)	0.486
Inadequate (≥5)	163 (76.9)	176 (82.2)	166 (78.3)		195 (77.7)	310 (80.1)	
Diuretics use, *n* (%)							
Yes	33 (15.6)	33 (15.4)	41 (19.3)	0.472	42 (16.7)	65 (16.8)	1.000
No	179 (84.4)	181 (84.6)	171 (80.7)		209 (83.3)	322 (83.2)	
Self-perception of health status, *n* (%)							
Very good/good	64 (30.2)	46 (21.5)	67 (31.6)	0.027	38 (15.1)	139 (35.9)	<0.001
Reasonable	103 (48.6)	113 (52.8)	113 (53.3)		131 (52.2)	198 (51.2)	
Bad/very bad	45 (21.2)	55 (25.7)	32 (15.1)		82 (32.7)	50 (12.9)	
Exhaustion (questions), *n* (%)							
Yes	87 (41.0)	95 (44.4)	69 (32.5)	0.036	–	–	–
No	125 (59.0)	119 (55.6)	143 (67.5)				
Free water reserve (L), *n* (%)							
First tertile (<0.306)	–	–	–	–	87 (34.7)	125 (32.3)	0.036
Second tertile (0.306–0.768)					95 (37.8)	119 (30.7)	
Third tertile (>0.768)					69 (27.5)	143 (37.0)	

IPAQ, International Physical Activity Questionnaire; MNA-SF, Mini-Nutritional Assessment – Short-Form.

tertiles of FWR and reported exhaustion in both sexes. These variables were used in the multivariate analysis. Salt intake and diuretic use were also included as potential confounders for both sexes.

Women ≥80 years old classified in the last tertile of FWR showed a decreased risk of perceived exhaustion (third tertile: OR = 0.34; 95% CI = 0.15–0.79) compared to women in the first FWR tertile. This association remained statistically significant even after being adjusted for confounders (third tertile: OR = 0.38; 95% CI = 0.15–0.96). No such significant association was observed in women aged <80 years, nor in men (Table 3).

The results were consistent with the primary analyses when participants with chronic back pain were excluded.

Discussion

The present study provides the first reported evidence on the relation between hydration status and self-reported exhaustion among older adults and shows that better hydrated oldest old women have a decreased risk of perceived exhaustion.

Although the role of water and hydration in physical functions has been of considerable interest to the scientific community, the effect of water and hydration on

Table 2 Sociodemographic, lifestyle, clinical, anthropometric and nutritional characteristics of 505 Portuguese older men (≥65 years old) according to FWR tertiles (L)

Participants' characteristics	First tertile, <0.107 L (*n* = 168)	Second tertile, 0.107–0.626 L (*n* = 169)	Third tertile, >0.626 L (*n* = 168)	*P*	With exhaustion (*n* = 127)	Without exhaustion (*n* = 378)	*P*
Age (years), *n* (%)							
65–79	144 (85.7)	131 (77.5)	134 (79.8)	0.140	101 (79.5)	308 (81.5)	0.695
≥80	24 (14.3)	38 (22.5)	34 (20.2)		26 (20.5)	70 (18.5)	
Marital status, *n* (%)							
Single/divorced/widowed	43 (25.6)	65 (38.5)	60 (35.7)	0.031	43 (33.9)	125 (33.1)	0.913
Married/common-law marriage	125 (74.4)	104 (61.5)	108 (64.3)		84 (66.1)	253 (66.9)	
Physical activity (IPAQ) (kcal week^{-1}), *n* (%)							
Normal (men <383; women <270)	156 (92.9)	136 (80.5)	146 (86.9)	0.004	97 (76.4)	341 (90.2)	<0.001
Low (men ≥383; women ≥270)	12 (7.1)	33 (19.5)	22 (13.1)		30 (23.6)	37 (9.8)	
Body mass index, *n* (%)							
Underweight/normal	26 (15.5)	32 (18.9)	33 (19.6)	0.146	19 (15.0)	71 (19.0)	0.066
Overweight	80 (47.6)	90 (53.3)	94 (56.0)		60 (47.2)	204 (54.0)	
Obesity	62 (36.9)	47 (27.8)	41 (24.4)		48 (37.8)	102 (27.0)	
Nutritional status (MNA-SF), *n* (%)							
Without undernutrition	149 (88.7)	153 (90.5)	149 (88.7)	0.819	105 (82.7)	346 (91.5)	0.008
With risk of undernutrition or undernourished	19 (11.3)	16 (9.5)	19 (11.3)		22 (17.3)	32 (8.5)	
Season urine sample collection, *n* (%)							
Autumn/winter	51 (30.4)	58 (34.3)	51 (30.4)	0.665	38 (29.9)	122 (32.3)	0.660
Spring/summer	117 (69.6)	111 (65.7)	117 (69.6)		89 (70.1)	256 (67.7)	
Salt intake (g), *n* (%)							
Adequate (<5)	7 (4.2)	21 (12.4)	12 (7.1)	0.018	12 (9.4)	28 (7.4)	0.452
Inadequate (≥5)	161 (95.8)	148 (87.6)	156 (92.9)		115 (90.6)	350 (92.6)	
Diuretics use, *n* (%)							
Yes	9 (5.4)	21 (12.4)	26 (15.5)	0.010	15 (11.8)	41 (10.8)	0.746
No	159 (94.6)	148 (87.6)	142 (84.5)		112 (88.2)	337 (89.2)	
Self-perception of health status, *n* (%)							
Very good/good	77 (45.8)	67 (39.6)	63 (37.5)	0.617	34 (26.8)	173 (45.8)	<0.001
Reasonable	74 (44.0)	82 (48.5)	84 (50.0)		64 (50.4)	176 (46.6)	
Bad/very bad	17 (10.1)	20 (11.8)	21 (12.5)		29 (22.8)	29 (7.7)	
Exhaustion (questions), *n* (%)							
Yes	38 (22.6)	49 (29.0)	40 (23.8)	0.357	–	–	–
No	130 (77.4)	120 (71.0)	128 (76.2)				
Free water reserve (L), *n* (%)							
First tertile (<0.306)	–	–	–	–	38 (29.9)	130 (34.4)	0.357
Second tertile (0.306–0.768)					49 (38.6)	120 (31.7)	
Third tertile (>0.768)					40 (31.5)	128 (33.9)	

IPAQ, International Physical Activity Questionnaire; MNA-SF, Mini-Nutritional Assessment – Short-Form.

psychomotor skills in older population is still unclear. One of the characteristics of the ageing process is a reduction of muscle strength, power and endurance. A recent study has demonstrated that hypohydration decreases muscle endurance by 8% and strength and aerobic power by 6% in younger adults [12]. Although data in older adults are scarce, the present study reveals that the participants who reported exhaustion were shown to be less physically active, which may be associated with difficulties at the muscle level. An appealing hypothesis to explain this relationship is that worse hydration may alter neuromuscular functions and performance as a result of an impaired excitation–contraction coupling [23]. In the ageing muscle, a reduced homeostatic capacity for intracellular calcium movement has been demonstrated to reduce contractile dysfunction [24,25]. This hypothesis led us to assume that hypohydration could be detrimental to muscle exercise capacity and exacerbate the effect of exhaustion in older adults. Otherwise, muscle mass, which is rich in fluid stores, decreases with ageing and leads to a reduced fluid reserve [5].

Although the construct underlying the definition of exhaustion used in the present study is based on physical issues, we cannot rule out the possibility that, in some situations, it may be interpreted as psychological.

Table 3 Binary logistic regression model results for the association between perceived exhaustion and FWR tertiles (L) and for 1143 Portuguese older adults (≥65 years old)

	65–79 years (n = 892)				≥80 years (n = 251)			
	Exhaustion				Exhaustion			
Free water eeserve	Crude OR (95% CI)	P trend	Adjusted OR (95% CI)	P trend	Crude OR (95% CI)	P trend	Adjusted OR (95% CI)	P trend
Women (n = 638)								
First tertile (n = 212)	1	0.656	1	0.759	1	0.014	1	0.049
Second tertile (n = 214)	1.14 (0.72–1.82)		1.09 (0.67–1.77)		1.29 (0.61–2.74)		1.07 (0.45–2.51)	
Third tertile (n = 212)	0.92 (0.58–1.46)		0.94 (0.58–1.52)		0.34 (0.15–0.79)		0.38 (0.15–0.96)	
Men (n = 505)								
First tertile (n = 168)	1	0.901	1	0.625	1	0.551	1	0.960
Second tertile (n = 169)	1.23 (0.71–2.11)		1.178 (0.67–2.08)		2.60 (0.73–9.22)		1.23 (0.27–5.58)	
Third tertile (n = 168)	0.97 (0.56-1.70)		0.875 (0.49-1.57)		1.80 (0.48-6.71)		1.11 (0.24–5.25)	

OR, odds ratio; CI, confidence interval.

In older adults, mild dehydration has also been revealed to be a predictor of progressive deterioration of cognitive function [26] and the feeling of exhaustion can be a consequence of cognitive or psychological exhaustion. It has been reported that hypohydration can influence cognitive status by producing disruptions in mood and cognitive functioning, such as concentration, alertness and short-term memory, in older adults [27]. The scientific literature indicates that a progressive impairment in short-term memory and visual function is exhibited once 2% of body fluid deficit is achieved in healthy adults subjects [2]. It was been proposed that physiological acute stressors such as mild dehydration compete for attention and awareness with parallel processes occurring in other cognitive domains compromises overall cognitive performance [26]. Nevertheless, research on this hypothesis is limited.

In the present study, we can observe a gender difference in hydration status, which is in accordance with the results from other populations [21] and reflects a lower intake of water in men. Other differences between sexes may contribute to explaining why the association between hydration and exhaustion was only found in women, such as the fact that men are physically more active and have a better muscular performance. On the other hand, self-perceived health status, which is a predictor of physical and psychological functioning, declines with age and varies by gender: psychological exhaustion appears to be more frequent in women [28].

There is some evidence that total water intake decreases with ageing [29]. A study from Volkert *et al.* (2005) showed that the oldest adults (≥85 years) had the lowest water intakes and, consequently, a worse hydration status [30], which is in line with the present study. Thus, because hypohydration can influence the self-perception of health status and cognition and the oldest women in general reveal a greater physical and psychological exhaustion, a condition of hypohydration can indirectly enhance the feeling of exhaustion.

Although a single period of 24-h urine collection may not represent an individual′s normal behaviour, it is expected that the mean values in large sample sizes, such as that employed in the present study, represent the group. In addition, 24-h urine is considered as the gold standard for assessing urine concentration [31]. Specifically, FWR is considered as a useful marker to quantify individual 24-h hydration status and identify subjects at risk of hypohydration [11]. It 'corresponds to the difference between the measured urine volume and the ideal urine volume necessary to excrete the actual 24-h urine solutes in subjects consuming a typical affluent Western type diet' [22]. In addition, having considered potential confounders such as taking diuretics, salt intake, physical activity and self-perception of health status were crucial when studying the association between hydration status and exhaustion. The present study was conducted with a sample of 1143 older adults and the possibility of type II error cannot be discarded. Also, the possibility that this sample can be biased towards a more responsive group of older adults cannot be ruled out because the recruitment methodology used did not allow us to calculate response rate and the reasons for refusal. Furthermore, the community of participants is a community that is likely to be healthier once it has become available to participate in the study and therefore can positively overestimate the self-perception of the health status of the Portuguese elderly population.

The importance of water to our health is crucial to understanding how some morbidities can be associated with hydration status. Several studies have demonstrated a positive effect of increasing water intake on physical and

cognitive functioning, which emphasises the role of hydration with respect to exhaustion status [26,27]. Even though causality cannot be established, the present study highlights the need for and the importance of deepening research on the association of hydration status and physical and cognitive function in relation to perceived exhaustion among older persons, in that hypohydration is a potentially modifiable risk factor. Preventing exhaustion involves providing a good hydration status, aiming for an adequate fluid intake, as well as the development of ways of screening that encourage older people and their caregivers to achieve and sustain an adequate hydration status.

The results obtained in the present study show an association between a worse hydration status and self-reported exhaustion in the oldest women among a group of older adults, highlighting the need to implement further studies clarifying this association.

Transparency declaration

The lead author affirms that this manuscript is an honest, accurate and transparent account of the study being reported. The reporting of this work is compliant with STROBE guidelines. The lead author affirms that no important aspects of the study have been omitted and that any discrepancies from the study as planned have been explained.

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Conflict of interests, source of funding, authorship

The authors declare that they have no conflicts of interest.
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PP, PM, AS, NB, CA and TA conceived the Nutrition UP project. PP and IA designed the study. IA and PP analysed the data and drafted the manuscript. All authors critically revised the manuscript and approved the final version submitted for publication.

References

1. Manz F & Wentz A (2003) 24-h hydration status: parameters, epidemiology and recommendations. *Eur J Clin Nutr* **57**(Suppl 2), S10–S18.
2. Gopinathan PM, Pichan G & Sharma VM (1988) Role of dehydration in heat stress-induced variations in mental performance. *Arch Environ Health* **43**, 15–17.
3. Popkin BM, D'Anci KE & Rosenberg IH (2010) Water, hydration, and health. *Nutr Rev* **68**, 439–458.
4. Bouby N & Fernandes S (2003) Mild dehydration, vasopressin and the kidney: animal and human studies. *Eur J Clin Nutr* **57**(Suppl 2), S39–S46.
5. Hooper L, Bunn D, Jimoh FO *et al.* (2014) Water-loss dehydration and aging. *Mech Ageing Dev* **136–137**, 50–58.
6. European Food Safety Authority (2010) Scientific opinion on dietary reference values for water. *EFSA J* **8**, 1459.
7. Michaud DS, Spiegelman D, Clinton SK *et al.* (1999) Fluid intake and the risk of bladder cancer in men. *N Engl J Med* **340**, 1390–1397.
8. Padez C, Padrão P, Macedo A *et al.* (2009) Caracterização do aporte hídrico dos portugueses. *Nutrícias* **25**, 7.
9. Lindeman RD, Tobin J & Shock NW (1985) Longitudinal studies on the rate of decline in renal function with age. *J Am Geriatr Soc* **33**, 278–285.
10. Ritz P & Berrut G (2005) The importance of good hydration for day-to-day health. *Nutr Rev* **63**, S6–S13.
11. Manz F & Wentz A (2005) Hydration status in the United States and Germany. *Nutr Rev* **63**, S55–S62.
12. Savoie FA, Dion T, Asselin A *et al.* (2015) Intestinal temperature does not reflect rectal temperature during prolonged, intense running with cold fluid ingestion. *Physiol Meas* **36**, 259–272.
13. Amaral TF, Santos A, Guerra RS *et al.* (2016) Nutritional strategies facing an older demographic: the nutrition UP 65 study protocol. *JMIR Res Protoc* **5**, e184.
14. Craig CL, Marshall AL, Sjostrom M *et al.* (2003) International physical activity questionnaire: 12-country reliability and validity. *Med Sci Sports Exerc* **35**, 1381–1395.
15. World Health Organization (2000) *Obesity: Preventing and Managing the Global Epidemic. Report of a WHO Consultation*. WHO Technical Report Series. pp. 1–253. Geneva: WHO.
16. Kaiser MJ, Bauer JM, Ramsch C *et al.* (2009) Validation of the Mini Nutritional Assessment short-form (MNA-SF): a practical tool for identification of nutritional status. *J Nutr Health Aging* **13**, 782–788.
17. Orme JG, Reis J & Herz EJ (1986) Factorial and discriminant validity of the Center for Epidemiological Studies Depression (CES-D) scale. *J Clin Psychol* **42**, 28–33.
18. Fried LP, Tangen CM, Walston J *et al.* (2001) Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* **56**, M146–M156.
19. ARUP Laboratories. Laboratory Test Directory—Creatinine, 24-h Urine. Salt Lake City, USA. http://ltd.aruplab.com/Tests/Pub/0020473 (accessed January 2019).
20. Stuver SO, Lyons J, Coviello A *et al.* (2017) Feasibility of 24-hr urine collection for measurement of biomarkers in community-dwelling older adults. *J Appl Gerontol* **36**, 1393–1408.

21. Manz F, Johner SA, Wentz A *et al.* (2012) Water balance throughout the adult life span in a German population. *Br J Nutr* **107**, 1673–1681.
22. Manz F, Wentz A & Sichert-Hellert W (2002) The most essential nutrient: defining the adequate intake of water. *J Pediatr* **141**, 587–592.
23. Bowtell JL, Avenell G, Hunter SP *et al.* (2013) Effect of hypohydration on peripheral and corticospinal excitability and voluntary activation. *PLoS ONE* **8**, e77004.
24. Weisleder N, Brotto M, Komazaki S *et al.* (2006) Muscle aging is associated with compromised Ca^{2+} spark signaling and segregated intracellular Ca^{2+} release. *J Cell Biol* **174**, 639–645.
25. Goulet ED, Melancon MO, Lafreniere D *et al.* (2018) Impact of mild hypohydration on muscle endurance, power and strength in healthy, active older men. *J Strength Cond Res* **32**, 3405–3415
26. Wilson MM & Morley JE (2003) Impaired cognitive function and mental performance in mild dehydration. *Eur J Clin Nutr* **57**(Suppl 2), S24–S29.
27. Suhr JA, Hall J, Patterson SM *et al.* (2004) The relation of hydration status to cognitive performance in healthy older adults. *Int J Psychophysiol* **53**, 121–125.
28. Alarcao V, Madeira T, Peixoto-Placido C *et al.* (2018) Gender differences in psychosocial determinants of self-perceived health among Portuguese older adults in nursing homes. *Aging Ment Health* 1–8.
29. Zizza CA, Ellison KJ & Wernette CM (2009) Total water intakes of community-living middle-old and oldest-old adults. *J Gerontol A Biol Sci Med Sci* **64A**, 481–486.
30. Volkert D, Kreuel K & Stehle P (2005) Fluid intake of community-living, independent elderly in Germany – a nationwide, representative study. *J Nutr Health Aging* **9**, 305–309.
31. Haussinger D, Lang F & Gerok W (1994) Regulation of cell function by the cellular hydration state. *Am J Physiol* **267**, E343–E355.

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OLDER ADULTS

Identifying older people at risk of malnutrition and treatment in the community: prevalence and concurrent validation of the Patients Association Nutrition Checklist with 'MUST'

J. L. Murphy[1] A. Aburrow,[2] A. Guestini,[1] R. Brown,[1] E. Parsons[2,3] & K. Wallis[2]

[1]Faculty of Health and Social Sciences, Bournemouth University, Bournemouth, UK
[2]Wessex Academic Health Science Network, Innovation Centre, Southampton Science Park, Chilworth, UK
[3]NIHR Biomedical Research Centre, University of Southampton, Southampton, UK

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Correspondence
Professor J. L. Murphy, Faculty of Health and Social Sciences, Bournemouth University, Royal London House, Christchurch Road, Bournemouth BH1 3LT, UK.
Tel.: +01202 962805
E-mail: jmurphy@bournemouth.ac.uk

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Abstract

Background: Despite policy guidance and quality standards, the majority of older adults with or at risk of malnutrition living in the community still remain under-detected and under-treated by health and social care professionals. The present study aimed to evaluate the concurrent validity of the Patients Association Nutrition Checklist against the 'Malnutrition Universal Screening Tool' ('MUST').
Methods: This cross-sectional study involved 312 older adults recruited from 21 lunch and social groups. All participants were screened as per standard methodology for 'MUST'. For the Patients Association Nutrition Checklist, they provided information about signs of unintentional weight loss in the past 3–6 months, experiencing loss of appetite or interest in eating. Chance-corrected agreement (κ) was assessed.
Results: Mean (SD) age of participants was 79.6 (8.3) years and body mass index was 27.8 (5.6) kg m^{-2}. The majority (n = 197; 63%) were living alone. Using 'MUST', the overall prevalence of malnutrition was 9.9% (n = 31) comprising 6.7% at medium risk and 3.2% at high risk. There were 21.8% of participants (n = 68) rated at risk of overall malnutrition by the Patients Association Nutrition Checklist. Moderate agreement was observed between the two tools ($\kappa = 0.47$, $P < 0.001$).
Conclusions: The Patients Association Nutrition Checklist has potential for early identification of malnutrition risk, attributed to unintentional weight loss and appetite changes with signposting to basic dietary advice and appropriate support. Further work is required to understand how this tool could be effectively used by stakeholders including volunteers, community workers and home care staff.

Introduction

With an ageing population across Europe [(1)], older adults over 65 years living in the community are at risk of malnutrition (as undernutrition) which stems from inter-related medical (disease-related), physical and social factors [(2)]. Currently, it is estimated that one in 10 people aged over 65 years in the UK are poorly nourished or at risk of malnutrition, equating to around one million older people [(3)]. Malnutrition is costly [(4)] and has many negative consequences that not only affect the individual, but also impose an enormous strain on healthcare resources as a result of delayed recovery from illness, increased need for health care provision at home, more frequent visits by nurses and a greater number of hospital admissions [(5,6)]. Malnutrition can be prevented by tackling both its causes and consequences

through screening and early intervention, and the benefits of treating malnutrition far outweigh the costs [7].

Many national and international guidelines recommend undertaking a simple nutrition screening procedure to identify those who are at risk [8–13]. Various nutrition screening tools have been validated to detect the risk of developing malnutrition in older adults [14]. Validated tools for use in community-living older adults include the 'Malnutrition Universal Screening Tool' ('MUST') [15], the Mini Nutritional Assessment Short Form (MNA-SF) [16], and the Seniors in the Community: Risk Evaluation for Eating and Nutrition (SCREEN II) [17]. The purpose of screening tools is to identify risk factors that may lead to the development of malnutrition and the need for further assessment [18].

Despite these different tools, malnutrition still remains under-detected and under-treated, with less focus on using validated tools for community-dwelling adults compared to screening in hospital settings [14]. Healthcare staff providing care and treatment within community settings who already review and manage older people are in a prime position to perform routine nutrition screening as part of practice [19]. Yet there remain constraints for identifying and treating malnutrition. The barriers faced by staff that impact on the incorporation of nutrition screening in their practice include limited time to screen and treat, low-prioritisation of nutrition, organisational culture, ease and acceptability of the 'MUST' screening tool, lack of knowledge and skills, improving communication between care settings [19,20]. Thus, there is a need to consider other approaches that could support and enable the identification of malnutrition. If older people could reliably be identified by a simple valid tool to highlight 'clinical concern', the tool could act as a prompt to screen using a validated screening tool such as the 'MUST' which would conform with National Institute of Health and Clinical Excellence clinical guidance [10]. As such, the tool could also have the potential to identify older people at risk earlier, help reduce growing health and social care costs and improve the quality of life for older people.

In recent years, the Patients Association has raised concerns about malnutrition in the UK and identified the need for a less 'clinical tool' which can be used in many settings to help encourage conversations about weight and nutrition and lead people towards established tools and guidance. In 2015, the Patients Association undertook a project working with the Malnutrition Pathway (Managing Adult Malnutrition in the Community) with an aim to produce a simple nutrition checklist for health and social care professionals to use with patients/carers and one for patients/carers [21]

Developed by the Patients Association with Dietitians, the early checklist was launched in December 2016 following extensive testing and modification with patients, relatives and with clinicians and volunteers working with older people [22]. Staff involved in the pilots said that the Patients Association Nutrition Checklist was simple and easy for anyone to use, was effective because it did not require devices for measuring weight and height or the ability to calculate percentages and has the benefit to start an informal conversation with people to identify risk and signposting as appropriate.

Working in collaboration with the Patients Association, the Wessex Academic Health Science Network Nutrition in Older People programme further developed this early version. They adapted it for use by people with care responsibilities including volunteers, community workers and home care staff to raise awareness and identify the risk of malnutrition with signposting to appropriate guidance and support for nutrition. It is primarily intended for people over 65 living in the community and has been pilot tested with several health, social care and voluntary sector providers. The final version was published in 2018 [22].

The present study aimed to investigate the concurrent validity of the Patients Association Nutrition Checklist against 'MUST' to assess whether the same people can be identified as malnourished. Concurrent validity involves comparison of the tool with another validated criterion measure and is assessed by kappa (κ), a chance-corrected measure or agreement. The 'MUST' was chosen because it is the most widely used validated screening tool by healthcare professionals to screen adults for malnutrition in the UK [23].

Materials and methods

Study design and participants

This cross-sectional study was conducted in community centres across Southern England between January and May 2018. Participants were excluded if they were <65 years, non-English speaking or unable to give informed consent. The Research and Ethics Committees of Bournemouth University and University of Southampton gave approval. Written informed consent was obtained from all the participants.

Nutrition screening tools

The 'MUST' [13] is designed for use across care and community settings and consists of a body mass index (BMI) category (BMI < 20 kg m^{-2} indicates at risk), a weight loss category (unintentional weight loss during the past 3–6 months; i.e. >5% indicates at risk) and an acute

disease effect score. A total score of one indicates medium risk (i.e. BMI 18.5–20 kg m^{-2} or unplanned weight loss 5%–10%) and a score of two or more is indicative of high malnutrition risk (i.e. either BMI < 18.5 kg m^{-2}, unplanned weight loss of >10% or BMI 18.5–20 kg m^{-2} and unplanned weight loss of 5%–10%). Height was measured to the nearest 0.1 cm using a portable, free-standing stadiometer (Seca Leicester stadiometer; Seca, Hamburg, Germany), in accordance with standard methodology [13]. Body weight was measured to the nearest 0.1 kg (calibrated SECA class III digital weighing scales were used and calibrated at the start of the study). BMI (kg m^{-2}) was calculated and scored from weight (kg) divided by the square of height (m^2) to determine BMI. Where weight and height were unable to be measured, mid upper-arm circumference was measured (using a tape measure) to provide a general indication of BMI score. Where height could not be measured, ulna length was measured using a tape measure.

The Patients Association Nutrition Checklist has two parts [22]. Section A has four key questions to focus discussions around weight loss (self-reported) and nutrition and aims to identify whether someone is 'at risk' of undernutrition. Section B consists of additional focussed questions on nutrition and eating and provides clear advice and signposting to appropriate support for older people living in the community. The four key questions (from Section A) were validated against 'MUST'.

Investigators and training

Two trained researchers (AA and AG) collected the nutrition screening data. One of the trained researchers was a registered dietitian (AA) and the other researcher (AG) has experience of working with older people in the community. The researchers administered the screening using both tools on the same occasion. The participants were asked to answer questions from Part A of the Patients Association Nutrition Checklist and were then screened using 'MUST'. Any of the participants identified to be at medium or high risk of malnutrition were provided with the Older People's Essential Nutrition leaflet [24] and advice to visit their general practitioner or practice nurse to discuss their screening result further. A measure of health-related quality of life was assessed using EQ-5D-3L [25].

Test–retest reliability of the Patients Association Nutrition Checklist

The test–retest reliability of the Patients Association Nutrition Checklist was assessed in a group of participants from the same community centres across Southern England as the main study between June and July 2019. The same exclusion criteria were used as the main study and all of the participants provided their written informed consent to participate in the study. The assessment using the Patients Association Nutrition Checklist was carried out at the beginning of the session and repeated either at the end of the session or at the next one they attended no more than 1 week later.

Statistical analysis

All analyses were carried out using SPSS, version 23.0 (IBM Corp., Armonk, NY, USA). Normally distributed continuous variables were presented as the mean (SD), whereas categorical variables are absolute and relative (%) frequencies. $P < 0.05$ (two-sided) was considered statistically significant. Kappa was used to determine the levels of agreement and chance-corrected agreement (κ) between 'MUST' and the Patients Association Nutrition Checklist. The following ranges of agreement (κ) were used: fair 0.21–0.4, moderate 0.41–0.6, substantive 0.61–0.8, and 0.81–1.00, almost perfect [26]. Power calculations suggested that, for an assumed malnutrition prevalence of 15%, a sample size of at least 300 people was needed to detect a chance-corrected agreement of $\kappa = 0.90$ with 80% power [confidence interval (CI) = 0.95, CI width 0.1] [27].

Results

Study population

The present study involved 312 participants from 21 lunch and social groups across Dorset ($n = 140$) and Hampshire ($n = 172$). Table 1 shows the demographic and anthropometric characteristics. Most (74.7%) of the participants were women and the mean (SD) age was 79.6 (8.3) years (range 65–84 years). There was an almost three-fold range in BMI (15.1–53.4 kg m^{-2}) and a mean (SD) BMI of 27.8 (5.6) kg m^{-2}. Participants were also asked to rate their

Table 1 Characteristics of the study participants ($n = 312$)

Variable	Mean (SD)	Range
Age	79.6 (8.6)	65–98
Female % ($n = 233$)	74.7	
Male % ($n = 79$)	25.3	
Weight (kg)	75.5 (55.5)	35.7–133.0
Height (m)	1.6 (0.1)	1.40–1.9
Body mass index	27.8 (5.6)	15.1–53.4
Wellbeing (1–10)	7.6 (1.7)	
Living status		
Alone % ($n = 200$)	64.1	
Other % (e.g. warden assisted) ($n = 4$)	1.3	
With Family % ($n = 23$)	7.4	
With Partner % ($n = 85$)	27.2	

wellbeing on a scale of 1–10, with 1 being their worst health score and 10 being their best health score. The mean (SD) wellbeing score using EQ-5D-3L was 7.6 (1.7) and the majority (n = 200; 64.1%) of participants were living alone, with the rest living with partner (27.2%), family (7.4%) and other (e.g. warden-assisted) (1.3%).

Prevalence of malnutrition using 'MUST'

The overall prevalence of malnutrition using 'MUST' was 9.9% (n = 31), comprising 6.7% at medium risk and 3.2% at high risk (Table 2). Of these participants 42% (n = 13) scored at step 1 BMI. The majority (69%, n = 9) scored 1 and 31% (n = 4) scored 2. There were 71% (n = 22) of participants who scored at step 2 for unintentional weight loss. There were 68% (n = 15) who scored 1 and 32% (n = 7) who scored 2.

Prevalence of malnutrition using Patients Association Nutrition Checklist

There were 21.8% of participants (n = 68) rated at risk of malnutrition by the Patients Association Nutrition Checklist (Table 3). Of these, 34% (n = 23) scored '*Yes*' or '*Don't know*' on question 1 (concerns about being underweight or need nutritional advice) and 44% (n = 30) scored '*Yes*' or '*Don't know*' on question 2 (loss of weight unintentionally in the past 3–6 months), 54% (n = 37) scored '*Yes*' or '*Don't know*' on question 3 (clothes or rings have become loose recently), and 56% (n = 38) scored '*Yes*' or '*Don't know*' on question 4 (recent loss of appetite and interest in eating). There were seven participants who answered '*don't know*' to at least one question. Of these, three answered '*yes*' to at least one other question of the four. There were only two participants (0.6%) who answered '*don't know*' to question 1, seven participants (2.2%) who answered '*don't know*' to question 2, and only one participant (0.3%) who answered '*don't know*' to question 4. None of the participants answered '*don't know*' to question 3.

Table 2 Assessment of malnutrition using 'MUST'

	n (%)
MUST malnutrition risk	
Overall prevalence	31 (9.9)
Medium risk = 1 (observe)	21 (6.7)
High risk = 2 (treat)	10 (3.2)
Step 1 BMI (kg m^{-2})	
Overall prevalence	13 (42)
Score of 1 only (18.5–20)	9 (69)
Score of 2 only (<18.5)	4 (31)
Step 2 unintentional weight loss	
Overall prevalence	22 (71)
Score of 1 only (5–10)	15 (68)
Score of 2 only (>10)	7 (32)

There were no step 3 acute disease scores. BMI, body mass index; 'MUST', Malnutrition Universal Screening Tool.

Table 3 Overall prevalence of malnutrition using Patients Association Nutrition Checklist: number of participants who answered 'yes' or 'don't know' to each question

	n (%)
Patients Association Nutrition Checklist malnutrition risk	
Overall prevalence	68 (21.8)
Scored yes to question 1: Concerns about being underweight or need nutritional advice	23 (34)
Scored yes or 'don't know' to question 2: Loss of weight unintentionally in past 3–6 months	30 (44)
Scored yes to question 3: Clothes or rings have become loss recently	37 (54)
Scored yes to question 4: Recent loss of appetite and interest in eating	38 (56)

Concurrent validity of the 'MUST' with the Patients Association Nutrition Checklist

The 'MUST' and Patients Association Nutrition Checklist showed a moderate level of agreement beyond chance within the range 0.41 to 0.60 (κ = 0.47 SE = 0.064; $P < 0.001$). Overall, there were 37 participants (11.9%) who were identified at risk using Patients Association Nutrition Checklist but were not identified for 'MUST' (Table 4). There were four discrepancies (12.9%) for the categorisation between 'MUST' and Patients Association Nutrition Checklist. On further exploration of the data, the reasons for the discrepancy were attributed to participants having no change in weight and that they had always been slim. Their 'MUST' scores were 1 and attributed to low BMI ranging from 18.7 to 19.9 kg m^{-2}.

Test–retest reliability of the Patients Association Nutrition Checklist

The test–retest reliability of the Patients Association Nutrition Checklist was conducted in 68 participants. The

Table 4 Cross-tabulation of malnutrition risk according to 'MUST' and Patients Association Nutrition Checklist

	n (%)
'MUST'	
No risk	281 (90.1)
At risk	31 (9.9)
Patients Association Nutrition Checklist	
No risk	244 (78.2)
At risk	68 (21.8)

overall test-retest reliability beyond chance was within the range 0.81–1.00, which indicates 'almost perfect' agreement ($\kappa = 0.90$ SE = 0.059; $P < 0.001$). For question 1, agreement beyond chance was within the range 0.81–1.00, which indicates 'almost perfect' agreement ($\kappa = 0.90$, SE = 0.098; $P < 0.001$). For question 2, agreement beyond chance was within the range 0.61–0.80, which indicates substantial agreement: ($\kappa = 0.68$ SE = 0.098; $P < 0.001$). For question 3, agreement beyond chance was within range of 0.81–1.00, which indicates 'almost perfect' agreement ($\kappa = 0.83$ SE = 0.095; $P < 0.001$). For question 4, agreement beyond chance was within the range 0.61–0.80, which indicates substantial agreement ($\kappa = 0.78$ SE = 0.123; $P < 0.001$).

Discussion

The present study has shown that the Patients Association Nutrition Checklist has moderate concurrent validity compared to 'MUST'. This level of agreement is consistent with malnutrition risk between 'MUST' and other tools in the same individuals [21].

Using 'MUST', the prevalence of malnutrition risk was 9.9% in this group of people living in the community, which compares favourably with measures of the prevalence of people at risk or having malnutrition of 10% in the community using 'MUST' [3]. However, there were 37 (11.9%) more people identified at risk using the Patients Association Nutrition Checklist compared to 'MUST'. The reasons for this could be attributed to identifying people in the earlier stages of weight loss and with appetite changes. The number of participants who were unable to recall whether they had experienced weight loss (2%) or who had reported loss of appetite (0.3%) was only very small. However, from the test–retest validation study, it was evident that the question asking whether participants lost a lot of weight unintentionally in the past 3–6 months did not show as strong chance agreement compared to the other questions (which was substantial or almost perfect), although the agreement was still acceptable.

Although 'MUST' has been extensively validated in hospitals, few studies have tested the validity of 'MUST' in community-dwelling older adults [14]. Other tools for screening malnutrition in the community have been validated such as SCREEN 11 with the purpose of screening for general nutritional status as well as a screening tool [17]. However, the Patients Association Nutrition Checklist was developed in response to the need for a new approach for the early identification of malnutrition risk, to elicit a conversation and that could be used by people with wider responsibility for nutrition that might include volunteers, community workers and home care staff people. Given the barriers to using already validated screening tools in the community [19,20], the Patients Association Nutrition Checklist offers opportunity to provide a way to identify 'clinical concern' for malnutrition risk at an early stage and/or lead to an indication of the need for 'MUST' screening in accordance with NICE by health and social care professionals [10,11].

Strengths and limitations

The Patients Association Nutrition Checklist is reliant on the participant's ability to recall weight loss, and who can report their appetite. Despite this, the number of people who were unable to provide this information in this study was very small. Almost all of the individuals who were approached and met the inclusion criteria agreed to participate in the study. However, we did not record details or the reasons for those who declined. We excluded people who were overtly not interested or overtly confused. A limitation of the test–retest reliability of the Patients Association Nutrition Checklist is the short time between the first and second assessment, which could have overestimated reliability because the participants might have remembered their previous score.

Conclusions

The Patients Association Nutrition Checklist not only demonstrates acceptable agreement compared to 'MUST' but also its potential for early identification of malnutrition risk in the community, which includes signposting to basic dietary advice and appropriate health and social care support within the tool. Further research is needed to understand how the Patients Association Nutrition Checklist could be effectively applied, including its ease of use by those other than health and social care staff, such as volunteers, community workers and home care staff.

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Conflict of interests, source of funding and authorship

The authors declare that they have no conflict of interests.
The source of funding for this study was from Bournemouth University.
JM, AA, KW and EP were responsible for the study conception and design. AA, AG and RB were responsible for data collection.

AG and JM analysed the data. JM, AA, KW and AG interpreted the data and contributed to the writing of the manuscript. JM had overall responsibility for the final content. All authors critically reviewed the manuscript and approved the final version submitted for publication.

Transparency declaration

The lead author affirms that this manuscript is an honest, accurate and transparent account of the study being reported and that no important aspects of the study have been omitted. The reporting of this work is compliant with STROBE guidelines.

References

1. European Commission (DG ECFIN) and Economic Policy Committee (Ageing Working Group) (2015) The 2018 Ageing Report: economic and budgetary projections for the 28 EU Member States (2016–2070). Institutional Paper 079. Available at: http://www.silvereco.org/en/wp-content/uploads/2018/06/the-2018-ageing-report.pdf (accessed 11 February 2019).
2. Ahmed T & Haboubi N (2010) Assessment and management of nutrition in older people and its importance to health. *Clin Interv Aging* **5**, 207–216.
3. European Nutrition for Health Alliance (2006) Malnutrition among Older People in the Community: Policy Recommendations. In association with BAPEN, ILCUK and Associate Parliamentary Food and Health Forum. Available at: http://www.bapen.org.uk/pdfs/malnut_in_the_community.pdf (accessed 11 February 2019).
4. Elia M (2015) The cost of malnutrition in England and potential cost savings from nutritional interventions (full report) by the British Association for Parenteral and Enteral Nutrition and National Institute for Health Research Southampton Biomedical Research. Available at: www.bapen.org.uk (accessed 10 January 2019).
5. Wilson L & Health RP (2013) A review and summary of the impact of malnutrition in older people and the reported costs and benefits of interventions. 1–30. Available at: https://ilcuk.org.uk/wp-content/uploads/2019/01/Costs-Benefits_Report_Jun13.pdf (accessed 17 February 2019).
6. British Association of Parenteral and Enteral Nutrition (2010) Malnutrition Matters – Meeting Quality Standards in Nutritional Care. Available at http://www.bapen.org.uk/pdfs/toolkit-for-commissioners.pdf (accessed 10 January 2019).
7. Edington J, Barnes R, Bryan F *et al.* (2017) A prospective randomised controlled trial of nutritional supplementation in malnourished elderly in the community: clinical and health economic outcomes. *Clin Nutr* **23**, 195–204.
8. Kondrup J, Allison SP, Elia M *et al.* (2003) ESPEN guidelines for nutrition screening 2002. *Clin Nutr* **22**, 415–421.
9. Mueller C, Compher C & Ellen DM (2011) ASPEN Board of Directors. ASPEN clinical guidelines. Nutrition screening, assessment and intervention in adults. *J Parenter Enteral Nutr* **35**, 16–24.
10. National Institute of Health and Clinical Excellence (NICE) (2006) Nutritional Support in Adults. Available at: http://www.nice.org.uk/nicemedia/live/10978/29978/29978.pdf (accessed on 20 January 2019).
11. National Institute of Health and Clinical Excellence (NICE) (2007) Nutrition support in adults. 1–26. Available at: http://www.nice.org.uk/nicemedia/live/10978/29978/29978.pdf%5Cnpapers3://publication/uuid/48F2C672-83ED-4CAB-9BDC-BB22A7C7D3A1 (accessed on 20 January 2019).
12. Council of Europe, Committee of Ministers (2003) *Resolution ReAP (2003) 3 on Food and Nutritional Care in Hospitals*. Strasbourg, France: Council of Europe. Available at: https://www.nutritionday.org/cms/upload/pdf/11.resolution/Resolution_of_the_Council_of_Europe.pdf (accessed on 17 February 2019).
13. Elia M (2012) The MUST Report. Nutritional screening of adults: a multidisciplinary responsibility. Executive Summary. Available at: http://www.bapen.org.uk/pdfs/must/must_exec_sum.pdf (accessed on 17 February 2019).
14. Power L, Mullaly D, Gibney ER *et al.* (2018) A review of the validity of malnutrition screening tools used in older adults in community and health care settings – a MaNuEl study. *Clin Nutr* **24**, 1–13.
15. Todorovic V, Russell C & Elia M (2011) The 'MUST' Explanatory Booklet. A Guide to the MUST for Adults. Malnutrition Action Group (MAG) a standing committee of BAPEN. Available at: http://www.bapen.org.uk/pdfs/must/must_explan.pdf (accessed on 17th January 2019).
16. Rubenstein LZ, Harker JO, Salva A *et al.* (2001) Screening for undernutrition in geriatric practice: developing the short form mini nutritional assessment (MNA-SF). *J Gerontol A Biol Sci Med Sci* **56**, M366–M372.
17. Keller HH, Goy R & Kane SL (2005) Validity and reliability of SCREEN II (Seniors in the community: risk evaluation for eating and nutrition, Version II). *Eur J Clin Nutr* **59**, 1149–1157.
18. Field LB & Hand RK (2005) Differentiating malnutrition screening and assessment: a nutrition care process perspective. *J Acad Nutr Diet* **115**, 824–828.
19. Green SM, James EP, Latter S *et al.* (2014) Barriers and facilitators to screening for malnutrition by community nurses: a qualitative study. *J Hum Nutr Diet* **27**, 88–95.
20. Bracher M, Steward K, Wallis K *et al.* (2019) Implementing professional behaviour change in teams under pressure – results from phase one of a prospective process evaluation (the Implementing Nutrition Screening in Community Care for Older People (INSCCOPe) project. *BMJ Open* **9**, e025966.
21. The Patients Association (2017) Managing Malnutrition in the Community - Patients Association. Available at:

www.patients-association.org.uk (accessed on 17 February 2019).
22. The Patients Association (2018) Pilot projects to develop and evaluate the Patients Association Nutrition Checklist. Available at: https://www.patients-association.org.uk/patients-association-nutrition-checklist-toolkit (accessed 10th January 2019).
23. Stratton RJ, Hackston A, Longmore D *et al.* (2004) Malnutrition in hospital outpatients and inpatients: prevalence, concurrent validity and ease of use of the 'Malnutrition Universal Screening Tool' ('MUST') for adults. *Br J Nutr* **92**, 799–808.
24. Wessex Academic Health Science Network. Older People's Essential Nutrition (OPEN) leaflet. Available at: http://wessexahsn.org.uk/open-leaflet.pdf (accessed 10th January 2019).
25. Herdman M, Gudex C, Lloyd A *et al.* (2011) Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Qual Life Res* **20**, 1727–1736.
26. Landis JR & Koch GG (1977) The measurement of observer agreement for categorical data. *Biometrics* **33**, 159–174.
27. Jones JM (2004) Validity of nutritional screening and assessment tools. *Nutrition* **20**, 312–317.

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OLDER ADULTS

The impact of home-delivered meal services on the nutritional intake of community living older adults: a systematic literature review

K. Walton,[1,2] V. A. do Rosario[1,2] H. Pettingill,[1] E. Cassimatis[1] & K. Charlton[1,2]

[1]School of Medicine, Faculty of Science, Medicine and Health, University of Wollongong, Wollongong, NSW, Australia
[2]Illawarra Health & Medical Research Institute, University of Wollongong, Wollongong, NSW, Australia

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Correspondence
V. A. do Rosario, School of Medicine, Faculty of Science, Medicine, and Health, University of Wollongong, Wollongong, NSW 2522, Australia.
Tel.:+61 2 4221 5197
E-mail: vadr998@uowmail.edu.au

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Abstract

Background: There is a global increase in populations aged over 65 years. Physiological changes that occur during ageing may increase the nutritional risk for older adults. To avoid malnutrition and address some of the barriers to obtain an adequate food supply, home-delivered meals services provide meals in the home or in congregate settings for older adults who require nutritional support.
Methods: This systematic literature review explored whether nutritional intake is improved in community-living older adults when receiving meal services compared to when meal services are not received. Four electronic databases were searched up to 31 January 2019. In total, 13 original studies were included in this analysis with the components: intervention of home-delivered meal or congregate meal services to older adults; comparison with groups not receiving meal services or days not receiving the meal service; and nutritional intake as an outcome measured by food history, dietary recall and/or food frequency questionnaire.
Results: The results supported a beneficial effect of home-delivered meals on dietary intake of energy, protein and/or certain micronutrients in older adults.
Conclusions: The increased total energy intake is a positive influence on malnutrition risk in frail older adults and the increased protein intake supports good health, promotes recovery from illness and assists in maintaining functionality in older adults. Additionally, there was a particular increase in calcium intake, which is relevant in ageing, especially for bone health.

Introduction

There is a global increase in populations aged over 65 years. The social and cultural aspects associated with this ageing phenomenon adversely impact on the ability of frail older adults to maintain adequate access to food [(1)]. Additionally, physiological changes that accompany the normal ageing process place older adults at increased nutritional risk [(2)].

Malnutrition is defined as a deficiency or imbalance in nutrient intake and has a relevant prevalence in community-living older adults, resulting in a worsening of health conditions, frailty and disability [(2)]. Given the multiple causes and consequences of malnutrition in older adults, it can be challenging to improve dietary intake. Shopping, cooking and eating independently can be a burdensome activity to older adults, particularly if living alone [(3)]. To address such barriers and to obtain adequate access to nutrition, various services are available to provide meals for older adults who require nutritional support [(4)]. Meals-on-Wheels (MOW), the most widely recognised of these home delivery meals (HDM) services, is a community-based not-for-profit organisation that operates in many countries. HDM can improve dietary intake,

especially when meals reach the most vulnerable individuals [3]. HDM also decreases institutionalisation of older adults and it is a potential mechanism for decreasing healthcare expenditure [5].

There are several types of HDM services that exist, with variations on how programmes operate, the services offered, the eligibility requirements of clients who can access the services, the type of meals delivered and whether there are provisions made for special dietary needs. Such services can be either provided individually at home or via congregate meals, in which meals are provided in group settings such as senior citizens centres, allowing people the opportunity to socialise when eating their meals [6].

Other studies have explored the association of such services with nutritional status, food safety and insecurity, dietary patterns, socio-emotional aspects, and several other outcomes [7,8]; however, an updated review exploring the impact of HDM on dietary intakes and its implication on older adults is lacking. Thus, the current systematic review of the scientific literature aimed to investigate whether dietary intake is improved in community-living older adults when receiving meal services compared to when meal services are not received.

Materials and methods

A systematic literature review was undertaken using the procedures outlined in the Evidence Analysis Manual: Steps in the Academy Evidence Analysis [9] and in the PRISMA statement [10]. The study selection, quality assessment, data extraction and synthesis were conducted independently by three researchers and then reviewed by all authors.

Search strategy

Four electronic databases were searched: Scopus, Medline, Science Direct and Web of Science. Various combinations of the following keywords were used: 'Meals on Wheels', 'Elderly Nutrition Program', 'home delivered meal', 'weekend meal', 'meal service', 'nutrient intake', 'nutritional intake', 'dietary intake' and 'nutritional risk'. All database searches were completed up to 31 January 2019.

Study selection criteria

Selection criteria were formed using the population intervention comparison outcome (PICOS) format [10]. These criteria were used to screen the titles and abstracts of literature returned via database searching. Study selection criteria included:

(i) participants: older adults living at home; (ii) interventions: home-delivered meal (HDM) or congregate meal services; (iii) comparators: a comparison group not receiving meal services or occasions where a meal service participant did not receive a meal; (iv) outcomes: nutritional intake measured by food history, dietary recall and/or food frequency questionnaire (FFQ); and (v) study design: cross-sectional, pre-post quasi-experimental and cohort studies.

Eligibility of articles for inclusion was extended to include only peer reviewed journal articles that were published in the English language, whereas review articles were excluded. After the removal of nonrelevant and duplicate articles, the remaining articles were retrieved for further evaluation of the full-text. Articles that met all study selection criteria were eligible for inclusion in the review. The study selection process was based on PRISMA guidelines and is outlined in Fig. 1 [6].

Data extraction and synthesis

A data extraction form was used to collate the characteristics from each study: author(s), year of publication, study design, study population, sample size, intervention (if applicable), comparison measure, outcome measure and study outcomes.

Study quality assessment

The quality of each study was assessed for scientific soundness using the Quality Criteria Checklist for Primary Research [5]. Study quality was determined by identifying the presence or absence of 10 validity criteria. An overall quality rating was then assigned to each study, according to positive, neutral or negative rankings.

Results

Study selection

In total, 867 articles were returned via database searching. Seventy-four duplicates were removed and 746 articles were excluded during title and abstract screening (Fig. 1). The full-text of the remaining 47 articles were accessed and evaluated against the study selection criteria. Thirty-four articles were excluded because they did not meet all criteria (Fig. 1) and the remaining 13 studies were eligible for the review.

Characteristics of the studies included in the review

The characteristics of the 13 studies reviewed are summarised in Table 1. Eight of the studies were cross-sectional in design [11–18], four were pre-post quasi-experimental studies [19–22] and one was a cohort study [23]. Eleven studies had relatively smaller sample sizes

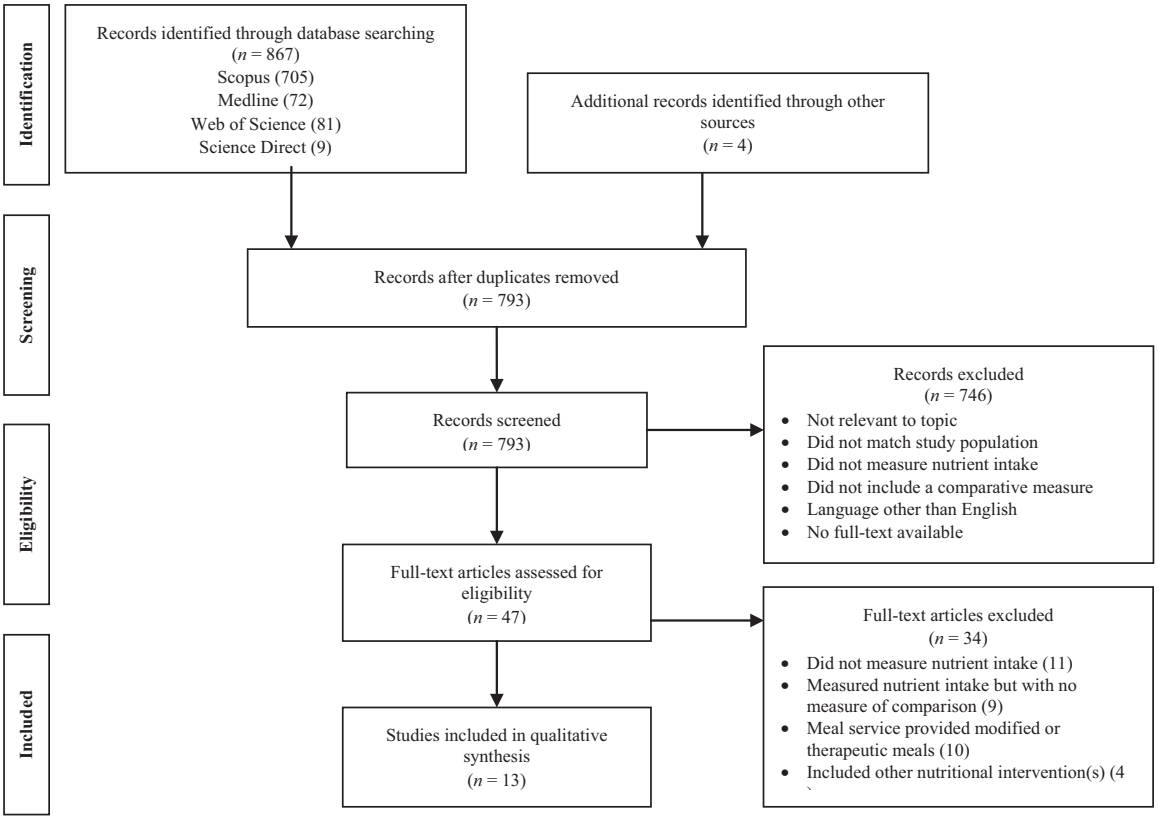

Figure 1 Study selection process.

ranging from 16 to 445 participants, wherea two of the studies obtained larger samples, ranging from 1065 to 2691 participants. The age categorisation used to classify older adults in the studies ranged from over 50 years to over 70 years. Two studies did not specify the age range used during recruitment [14,16], whereas one study recruited adults aged >18 years but specified a sub-category of adults >60 years [11], with this comprising the sub-group of data reported in the present review.

In the cohort study [23] and four pre-post studies [19–22], participants commenced the use of HDM services at recruitment to the study, whereas all other cited studies investigated the dietary intake of existing participants enrolled in HDM or congregate meal services as the independent variable. Four studies used a single group of participants as their own control and made comparisons between the nutrient intakes on occasions when meals were and were not received [11,14,18,21]. Five studies [12,13,15–17] compared the nutrient intakes of two separate groups who were either participating in a meal programme or not. Two studies combined both methods and made comparisons between those participating in a meal programme (either on a meal or non-meal day) and those who had never participated in a meal programme [22,23]. Regarding the type of meal programme, three studies included participants receiving congregate meal services [13,15,17], whereas all others were traditional HDM services.

A food record was the only method used for measuring nutrient intake in two studies [17,20], whereas another study used only a FFQ [19]. All other studies used a 24-h dietary recall method, although two studies also combined this with a FFQ [15] or a FFQ and a 1-day food record [16]. The frequency of data collection within studies ranged from one occasion to seven occasions. Four studies measured the impact of participation in a meal programme over time where the length of intervention ranged from 8 weeks to 12 months [20–23].

Study quality

One study received a positive overall quality rating [11] and one study received a negative rating [14], whereas all others received a neutral quality rating. This was mainly the result of a number of factors related to the study design (e.g. no inclusion of randomised clinical trials) and a lack of information reported in the studies, particularly for the questions related to validity, as shown in Table 2.

Table 1 Characteristics and outcomes of included studies

Author(s); year; Country	Study design	Population	Sample size	Intervention	Comparison	Outcome measure	Outcomes
An; 2015; USA [11]	Cross-sectional	Adults >18 years participating in HDM programme	106	Existing use of HDM service	HDM day and non-HDM day	24-h dietary recall (two nonconsecutive days)	On days of service use there was a significant net increase in the daily intake of protein (8.39 g, SE: 4.55), fibre (3.39 g, SE: 1.06), calcium (145.94 m, SE: 58.19), copper (0.16 mg, SE: 0.06), magnesium (45.37 mg, SE: 13.93), potassium (317.39 mg, SE: 139.81), selenium (14.04 mg, SE: 5.98), and sodium(327.52 mg, SE: 160.91). There was no significant effect on the daily intake of energy, fat and vitamin D
Steele & Bryan; 1985; USA [12]	Cross-sectional	Home-bound adults >60 years	54	Existing use of HDM service	Participation and nonparticipation in HDM service	24-h dietary recall	There was no significant difference between HDM participants and nonparticipants intake of energy, protein, fat, or other vitamins and minerals
Frongillo & Wolfe; 2010; USA [23]	Cohort	Adults >60 years newly referred to HDM or other non-meal care services	100	Commencing use of HDM service	HDM day, non-HDM day, and nonparticipation in HDM service	24-h dietary recall (baseline, 6-months and 12-months)	At 6 months the HDM group had significantly greater intake of energy ($\beta = -283$, $P = 0.04$), protein ($\beta = -16.2$, $P < 0.01$), vitamin A (-0.67, $P = 0.02$), thiamine ($\beta = -0.39$, $P = 0.02$), riboflavin (β-0.66, $P \leq 0.01$), vitamin B_6 ($\beta = -0.58$, $P = 0.01$), vitamin B_{12} ($\beta = -0.63$, $P = 0.02$), calcium ($\beta = -232$, $P = 0.03$) and zinc ($\beta = -4.01$, $P = 0.01$) compared to the HDM group not receiving a meal on the day of recall. At 12 months, the HDM group had significantly greater intake of energy ($\beta = -501$, $P \leq 0.01$), protein ($\beta = -27.7$, $P < 0.01$), vitamin A (-0.57, $P = 0.02$), thiamine ($\beta = -0.39$, $P = 0,02$), riboflavin (β-0.57, $P = 0.02$), vitamin B_6 ($\beta = -0.47$, $P = 0.01$), vitamin B_{12} ($\beta = -0.95$, $P = 0.01$) and zinc ($\beta = -3.17$, $P < 0.01$) compared to the HDM group not receiving a meal on the day of recall. At 6 months, the HDM group had significantly greater intake of vitamins A ($\beta = -0.56$, $P = 0.03$), B_6 ($\beta = -0.32$, $P = 0.04$), B_{12} ($\beta = -0.50$, $P = 0.03$), D ($\beta = -1.45$, $P = 0.03$), E ($\beta = -0.35$, $P = 0.05$) and calcium ($\beta = -236$, $P = 0.02$), magnesium ($\beta = -45.4$, $P = 0.01$) and phosphorous ($\beta = -259$, $P = 0.01$) compared to the nonparticipant group. There was no significant difference between these groups at 12 months
Roy & Payette; 2006; Canada [22]	Pre-post	Nonrecipients of MOW >65 years	51	Commencing use of HDM service	Before and after receiving HDM, and nonparticipation in HDM service	24 hr dietary recall on two consecutive days (pre-test) and five nonconsecutive days (post-test, 8-weeks)	HDM group had significantly higher intake of energy (121 kcal, $P = 0.05$), protein (7.4 g, $P = 0.03$), lipid (7.9 g, $P = 0.03$) and thiamine (0.2 mg, $P = 0.03$) after 8 weeks of programme use compared to nonparticipants in HDM programme
Millen *et al.*; 2002; USA [13]	Cross-sectional	Adults >60 years participating in ENP and matched nonparticipant sample	2691	Existing use of HDM or congregate meal service	Participation and nonparticipation in HDM or congregate meal service	24-h dietary recall	ENP participants had significantly ($P > 0.001$) higher intakes of energy (8.5%), protein (8.3%), vitamins A (24.6%), C (13.6%), D (30.6%), E (14.1%), thiamine (5.9%), riboflavin (15.6%), niacin (6.1%), B_6 (8.9%), folate (8.3%), calcium (24.2%), magnesium (14.3%), zinc (12.0%) and phosphorous (14.5%)

Table 1 Continued

Author(s); year; Country	Study design	Population	Sample size	Intervention	Comparison	Outcome measure	Outcomes
Walden *et al.*; 1989; USA [14]	Cross-sectional	Older adults participating in HDM programme	16	Existing use of HDM service	HDM day and non-HDM day	24-h dietary recall (meal delivery day and non-meal delivery day)	HDM participants had significantly lower intake of energy, carbohydrate and fat on weekends when they did not receive a meal compared to on weekdays when a meal was received ($P < 0.05$)
Heuberger & Wong; 2014; USA [15]	Cross-sectional	Women >60 years who were depressed, widowed, or both	1,065	Existing use of HDM or congregate meal service	Participation and nonparticipation in HDM or congregate meal service	24-hr dietary recall and food frequency questionnaire	The use of congregate and/or home-delivered meals made no significant contribution to the intake of any nutrient.
Kohrs *et al.*; 1980; USA [16]	Cross-sectional	Older adults participating in ENP	445	Existing use of HDM service	Participation in HDM programme 2–5 times per week, <2 times per week or 0 times per week	24-h dietary recall, 1-day food record and diet history using food frequencies	There was no significant association between frequency of programme participation and long-term energy intake. Frequency of participation was significantly associated with dietary intake of riboflavin and thiamine ($P < 0.05$)
Neyman *et al.*; USA; 1996 [17]	Cross-sectional	Adults >60 years	135	Existing use of congregate meal service	Participation and nonparticipation in congregate meal programme	3-day food record (2 week days and 1 weekend day)	There was no significant difference in the nutrient intake of participants on days when they ate at the meal programme and the days when they did not. There was no significant difference in the nutrient intakes of participants and nonparticipants
Wright *et al.*; 2015; USA [21]	Pre-post	Adults >55 years newly enrolled in MOW service	62	Commencing use of HDM service	Before and after receiving HDM	24-h dietary recall (baseline and 2-months)	There was a significant increase in participants' energy (355.06 kcal, $P < 0.0005$) and protein (19.63 g, $P < 0.0005$) intake between baseline and 2-months. No other nutrients were assessed
Denissen *et al.*; Netherlands; 2016 [20]	Pre-post	Adults >70 years unable to prepare their own dinner	44	Commencing use of HDM	Participation and nonparticipation in HDM service	2-day food record (baseline and 3-months)	HDM group had significant higher intake of calcium (115 mg, $P = 0.02$) compared to control group
Ullevig *et al.*; USA; 2018 [19]	Pre-post	Adults >60 years	49	Commencing use of HDM	Participation and nonparticipation in HDM service	153-item Food Frequency Questionnaire (baseline and 3-months)	HDM group had a significant ($P < 0.001$) increase in numbers of participants that met or exceeded the recommended dietary allowances for magnesium (8 participants, 18.6% increase) and zinc (10 participants, 23.2% increase)
Walton *et al.*; Australia; 2015 [18]	Cross-sectional	Adults >50 years	42	Existing use of HDM service	HDM day and non-HDM day	24-h dietary recall (meal delivery day and non-meal delivery da)	On HDM service days, there was an increase in daily energy intake in women (126.7 kcal, $P = 0.045$), but not overall neither in men compared to non-HDM day. There were no significant changes in protein intake

β, regression coefficient; ENP, elderly nutrition programme; MOW, meals on wheels.

Table 2 Study quality criteria checklist and rating

	An, 2015 [11]	Steel & Bryan, 1985 [12]	Frongillo & Wolfe, 2010 [23]	Roy & Payette, 2006 [22]	Millen *et al.*, 2002 [13]	Walden *et al.*, 1989 [14]	Heuberger & Wong, 2014 [15]	Kohrs *et al.*, 1980 [16]	Neyman, *et al.*, 1996 [17]	Wright *et al.*, 2015 [21]	Denissen *et al.*; 2016 [20]	Ullevig *et al.*; 2018 [19]	Walton *et al.*; 2015 [18]
Overall Quality Rating	+	Ø	+	Ø	Ø	-	Ø	Ø	Ø	Ø	Ø	Ø	Ø
Validity questions													
1. Was the research question clearly stated?	y	y	y	y	y	y	y	y	y	y	y	y	y
2. Was the selection of study subjects/patients free from bias?	y	n	y	n	y	n	n	n	n	n	n	n	n
3. Were study groups comparable?	y	n	y	y	n	n	n	n	n	n	n	n	n
4. Was the method of handling withdrawals described?	n	n	y	y	y	n	y	y	n	y	y	y	n
5. Was blinding used to prevent introduction of bias?	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
6. Were intervention/ therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were intervening factors described?	y	n	n	y	n	n	n	y	n	n	y	n	y
7. Were outcomes clearly defined and the measurements valid and reliable?	y	y	y	y	y	y	y	y	y	y	y	y	y
8. Was the statistical analysis appropriate for the study design and type of outcome indicators?	y	y	y	y	y	n	y	y	y	y	y	y	y
9. Were conclusions supported by results with biases and limitations taken into consideration?	y	y	y	y	y	n	y	y	y	y	y	y	y
10. Is bias due to study's funding or sponsorship unlikely?	n	y	n	y	y	n	y	y	n	n	y	y	y

+, positive; -, negative; Ø, neutral; y, yes; n, no; u, unclear; NA, not applicable.

Outcomes of meal service programmes

Protein and energy were the only nutrients measured in all studies, where improvements associated with meal delivery services were reported in six studies [11,13,14,18,21–23]. Three of five studies that showed improvements in protein intake were those in which the meal delivery commenced within the trial period [21–23], whereas the two other studies found higher intakes of existing HDM service clients on days where a meal was received compared to a non-HDM day [11], or between participants and nonparticipants of the service [13]. An increase in energy intake was found in five studies [13,14,21–23], with four of these also reporting a simultaneous increase in protein intake [13,21–23]. The findings for energy intake were similar to those for protein, such that the studies introducing an HDM service [21–23] performed best, followed by the two studies that compared meal and non-meal days in existing clients [14] or participants versus nonparticipants [13]. Additionally, another study reported an increase in energy intake, although only in women, comparing a MOW and a non-MOW day [18].

In relation to micronutrient intake, seven of 12 studies [13,15,16,19,20,22,23] that assessed this outcome found increased intake for at least one vitamin [11,13,16,22,23] and/or mineral [11,13,19,20,23], whereas three studies reported an increase in more than five micronutrients [11,13,23]. Three of the 13 studies included in this review did not find improvements in dietary intake associated with participation in a HDM service for either energy, protein, other macronutrients or micronutrients [12,15,17]. Two of these studies [15,17], related to congregate meal services, had limited result details.

Discussion

The aim of this systematic literature review was to explore whether dietary intake is improved in community-living older adults when receiving meal services compared to when meal services are not received. The review identified 13 eligible studies, which presented cross-sectional, pre-post quasi-experimental and cohort studies designs. The results supported a beneficial effect of home-delivered meals on improvements in dietary intake of energy, protein and/or certain micronutrients (calcium, vitamin A, B complex vitamins, vitamin D, zinc, magnesium and others) in older adults.

Physiological changes that occur during the normal ageing process modify nutritional requirements in older adults and are determined by various factors, such as ingestion, digestion and absorption of nutrients; thus, energy expenditure and caloric requirements may be altered [2]. Additionally, factors related to the inability of providing one's own meals, such as a lack of resources and access to food, disability or limited mobility, are usually eligibility requirements for populations that have access to HDM services. Therefore, the risk of malnutrition in these older adults is usually linked to an inability to access sufficient food to meet nutrient requirements, including total energy intake. Hence, the increased energy intake associated with home-delivered meals found in five studies [11,13,14,18,21–23] can be considered as a beneficial outcome to assist in reducing malnutrition risk in frail older adults. Higher protein requirements in older age are recommended to support good health, promote recovery from illness and maintain functionality in older adults via prevention of sarcopenia [24]. Inadequate protein intake is recognised as a determinant of frailty [25,26], as well as being associated with an increased risk of falls [27] in the older population. Recent evidence suggests that a dietary intake of 1.0–1.3 g protein kg^{-1} is required to optimise physical function, particularly when undertaking resistance exercise recommendations and/or to compensate for the inflammatory and catabolic conditions associated with chronic and acute diseases [24]. It is well recognised that older adults often consume less protein than younger adults [24,28] and also that the anabolic response to protein is often blunted in ageing [29,30]; thus, the findings of increased protein intake from five of the studies included in the present review are promising.

Studies that reported improvements in both energy and protein intake in HDM recipients were more likely to be those in which new, rather than existing, clients were investigated [21–23]. Older adults commencing the use of a HDM service are likely to be at greater nutritional risk than those who have been receiving support for some time. All three studies that did not present significant results had interventions with people already utilising HDM [12,15,17]. Nonetheless, the other study [23] reporting improvements not only for energy and protein intake, but also for several micronutrients was the one that recruited a nationally representative sample of participants. In addition, the same study found that HDM services (both home-delivered and congregate meals) provided 75% of older people's daily energy requirements and between 30% and 50% of their daily nutrient intake, whereas the mean daily nutrient intake approached or exceeded the recommended daily allowances for 11 of 16 nutrients examined. The meals served in this successful programme were produced in accordance with the dietary guidelines for its population and met the nutritional requirements established.

In relation to micronutrients, insufficient dietary intake of several nutrients has been reported in older community adults (vitamins A, B_{12}, D and zinc), with a higher prevalence in long-term care facilities (vitamins A, D and E) [31].

In Europe, USA and Canada, deficiencies in dietary intake of one or more nutrients are present in 35% of individuals aged 50 years or older [32]. A higher life expectancy may lead to higher risk of deficiency, especially for vitamins B_{12}, A, C, and D, iron, calcium and folate [33]. In addition, a lower food intake has been associated with lower intakes of calcium, iron, zinc, B vitamins and vitamin E [32]. Despite the numerous nutritional issues present in ageing, recommended dietary allowances for older adults are mostly similar [34]. However, some micronutrients have high dietary intake requirements such as calcium, vitamins D and B_6, whereas others, even presenting equal requirements, are crucial for healthy aging and are associated with lower intake in older adults such as vitamin B_2 (riboflavin), folic acid and vitamin B_{12} [2,32–34]. Seven studies included in this review found positive results in at least one micronutrient when comparing older adults with and without HDM services [11,13,16,19,20,22,23]. In particular, the increase in calcium intake found in four studies [11,13,20,23] has an important relevancy in ageing, especially for bone health. This micronutrient usually presents an impaired absorption as a result of changes gastrointestinal tract in ageing, which is enhanced if there is a concomitant vitamin D deficiency. Individuals between 70 and 90 years of age absorb approximately one-third less calcium than younger adults [2,32]. The decrease in kidney function to retain calcium decreases may also affect its reabsorption, as well as a decreased efficiency of the kidneys to convert vitamin D into its most active form (i.e. 1,25 dihydroxyvitamin D) may be present [2,35]. Only two studies [13,23] included in this review found an improvement in vitamin D intake, and such a modest result might been influenced by the high rates of supplementation of this vitamin in this age range.

Several other studies have evaluated the effects of home-delivered meals in older adults grouping studies of various designs, including a review that included pooled results from 13 quasi-experimental studies providing HDM interventions, including between-meal snacks, more food choices and provision of nutrition advice. Overall, these interventions improved nutrition and functional status, hospital readmission rates and quality of life [8]. A further similar review was conducted by Zhu *et al.* [7], who evaluated the impact of HDM services on diet and nutrition among recipients but included a wider range of outcomes such as effectiveness of home-delivered meal services, food insecurity and dietary patterns. In accordance with the review reported in the present study, six of eight studies included in their study found that HDM programmes significantly improved diet quality, increased nutrient intakes, and reduced food insecurity and nutritional risk among participants. Other beneficial outcomes include increased socialisation opportunities, an improvement in dietary adherence and a higher quality of life. Although these topics were not evaluated in this review, food safety and social connections related to HDM are relevant to this discussion. HDM clients are especially vulnerable to food-borne illness as a result of a high prevalence of health conditions that can suppress the immune system [36]. A food safety course for more than 1500 staff and volunteers with HDM programmes reported the most important food safety information concerned meal delivery and client handling of meals, especially with respect to ensuring that meals were kept at appropriate temperatures, as well as checking clients' refrigerator temperatures, adding labels with reheating instructions, checking use-by dates and instructing drivers not to leave meals at clients' doors [37]. Other positive results were found in a study that used the USDA Six-Item Food Security Scale to identify food-insecure households and households with very low food security. Two months after starting the HDM programme, there was an overall improve of 41.2% of participants' food security level, with 15.7% moving from very low to high food secure [21]. Loneliness and well-being also were significantly improved. Studies employing a qualitative approach found that HDM clients appear to have benefits that are beyond the actual meal itself, with the drivers providing additional support to their clients and the social bonds between drivers and clients strengthening over time [38]. In addition to the social contact, HDM may also help to restimulate an interest in meals and regularising mealtimes [39].

A number of factors may contribute to the discrepancies in the results within studies. First, certain outcomes are not comparable as a result of differences in study design and methods. For example, some studies examined differences in nutrient intake within the same individuals, whereas other studies made comparisons between those receiving meals and not receiving meals. A limitation of all studies was that they did not provide any information about the nutritional composition of the meals received by participants. Additionally, there was often little description of details, such as the type or frequency of meals received, the amount of the meal consumed on the day of dietary recall or to what degree the meal contributed to the participant's total dietary intake for that day. Further consideration of the impact of these variables is required to improve the validity of results. Furthermore, the majority of studies did not focus on whether participants met the recommended dietary requirements for optimal health, even if they had increased their nutrient intakes, making this issue an important need with respect to further research in this area. The level of results details also varied among the studies, which made it difficult to present a more homogeneous set of results. Still, regarding the methodology limitations of this review, only articles in English were

screened, which excludes many potential articles that, in this area of knowledge, are often published in the native language of its country. Only one included study was conducted in a country that does not have the English as native language [20].

The search of the current review did not return any randomised controlled trials because ethically meal services cannot be randomly allocated to one population and withheld from another. The use of blinding within studies to reduce bias is also not possible in the case of meal provision. Furthermore, the method of data collection in the studies relied on recall by participants and the accuracy of this information may be impacted by error in memory or conceptualisation of food portions, as well as it being subject to under- or over-reporting.

Conclusions

Home-delivered meal services are able to promote beneficial results in nutritional intake in community-living older adults. This review summarised the results of 13 studies and found a relevant increase in the dietary intake of energy and protein, as well as micronutrients such as calcium, vitamin A, B complex vitamins, vitamin D, zinc and magnesium. This indicates that these services can address the food access pillar of food security in this population, thus decreasing the risk of malnutrition and related harmful conditions.

Transparency declaration

The lead author affirms that this manuscript is an honest, accurate and transparent account of the study being reported. The reporting of this work is compliant with PRISMA guidelines [10]. The lead author affirms that no important aspects of the study have been omitted and that any discrepancies from the study as planned have been explained (Prospero registration number: CRD42017070495).

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Conflict of interests, sources of funding and authorship

The authors declare that they have conflicts of interest.
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References

1. United Nations, Department of Economics and Social Affairs, Population Division. World population ageing, 2017 highlights, 2017.
2. Bernstein M & Munoz N (2012) Position of the Academy of Nutrition and Dietetics: food and nutrition for older adults: promoting health and wellness. *J Acad Nutr Diet* **112**, 1255–1277.
3. Whitelock Emily & Ensaff Hannah (2018) On your own: older adults' food choice and dietary habits. *Nutrients* **10**, 413.
4. Sahyoun NR & Vaudin A (2014) Home-delivered meals and nutrition status among older adults. *Nutr Clin Pract* **29**, 459–465.
5. Thomas KS & Mor V (2013) Providing more home-delivered meals is one way to keep older adults with low care needs out of nursing homes. *Health Aff (Millwood)* **32**, 1796–1802.
6. Gualtieri MC, Donley AM, Wright JD *et al.* (2018) Home delivered meals to older adults: a critical review of the literature. *Home Healthc Now* **36**, 159–168.
7. Zhu H & An R (2013) Impact of home-delivered meal programs on diet and nutrition among older adults: a review. *Nutr Health* **22**, 89–103.
8. Campbell AD, Godfryd A, Buys DR *et al.* (2015) Does participation in home-delivered meals programs improve outcomes for older adults?: results of a systematic review. *J Nutr Gerontol Geriatr* **34**, 124–167.
9. Evidence Analysis Manual Academy of Nutrition and Dietetics, 2016[Internet]. [cited 2019 June 2]. Available from: https://www.andeal.org/vault/2440/web/files/2016_April_EA_Manual.pdf
10. Liberati A, Altman DG, Tetzlaff J *et al.* (2009) The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *PLoS Med* **6**, e1000100.
11. An R (2015) Association of home-delivered meals on daily energy and nutrient intakes: findings from the national health and nutrition examination surveys. *J Nutr Gerontol Geriatr* **34**, 263–272.
12. Steele MF & Bryan JD (1986) Dietary intake of homebound elderly recipients and nonrecipients of home-delivered meals. *J Nutr Elder* **5**, 23–34.
13. Millen BE, Ohls JC, Ponza M *et al.* (2002) The elderly nutrition program: an effective national framework for preventive nutrition interventions. *J Am Diet Assoc* **102**, 234–240.

14. Walden O, Hayes PA, Lee DY *et al.* (1989) The provision of weekend home delivered meals by state and a pilot study indicating the need for weekend home delivered meals. *J Nutr Elder* **8**, 31–43.
15. Heuberger R & Wong H (2014) The association between depression and widowhood and nutritional status in older adults. *Geriatr Nur* **35**, 428–433.
16. Kohrs MB, Nordstrom J, Plowman EL *et al.* (1980) Association of participation in a nutritional program for the elderly with nutritional status. *Am J Clin Nutr* **33**, 2643–2656.
17. Neyman MR, Zidenberg-Cherr S & McDonald RB (1996) Effect of participation in congregate-site meal programs on nutritional status of the healthy elderly. *J Am Diet Assoc* **96**, 475–483.
18. Walton K, Charlton KE, Manning F *et al.* (2015) The nutritional status and energy and protein intakes of MOW clients and the need for further targeted strategies to enhance intakes. *Appetite* **95**, 528–532.
19. Ullevig SL, Sosa ET, Crixell S *et al.* (2018) Impact of Home-Delivered meals on nutrition status and nutrient intake among older adults in central Texas. *J Nutr Health Aging* **22**, 861–868.
20. Denissen KFM, Janssen LMJ, Eussen SJPM *et al.* (2017) Delivery of nutritious meals to elderly receiving home care: feasibility and effectiveness. *J Nutr Health Aging* **21**, 370–380.
21. Wright L, Vance L, Sudduth C *et al.* (2015) The impact of a home-delivered meal program on nutritional risk, dietary intake, food security, loneliness, and social well-being. *J Nutr Gerontol Geriatr* **34**, 218–227.
22. Roy M-A & Payette H (2006) Meals-on-wheels improves energy and nutrient intake in a frail free-living elderly population. *J Nutr Health Aging* **10**, 554–560.
23. Frongillo EA & Wolfe WS (2010) Impact of participation in home-delivered meals on nutrient intake, dietary patterns, and food insecurity of older persons in New York state. *J Nutr Elder* **29**, 293–310.
24. Bauer J, Biolo G, Cederholm T *et al.* (2013) Evidence-based recommendations for optimal dietary protein intake in older people: a position paper from the PROT-AGE Study Group. *J Am Med Dir Assoc* **14**, 542–559.
25. Coelho-Júnior HJ, Rodrigues B, Uchida M *et al.* (2018) Low protein intake is associated with frailty in older adults: a systematic review and meta-analysis of observational studies. *Nutrients.* **10**, E1334.
26. Lorenzo-López L, Maseda A, de Labra C *et al.* (2017) Nutritional determinants of frailty in older adults: a systematic review. *BMC Geriatr* **17**, 108.
27. Zoltick ES, Sahni S, McLean RR *et al.* (2011) Dietary Protein Intake and subsequent falls in older men and women: the Framingham study. *J Nutr Health Aging* **15**, 147–152.
28. Robinson S, Reginster J, Rizzoli R *et al.* (2018) Does nutrition play a role in the prevention and management of sarcopenia? *Clin Nutr* **37**, 1121–1132.
29. Katsanos CS, Kobayashi H, Sheffield-Moore M *et al.* (2005) Aging is associated with diminished accretion of muscle proteins after the ingestion of a small bolus of essential amino acids. *Am J Clin Nutr* **82**, 1065–1073.
30. Wall BT, Gorissen SH, Pennings B *et al.* (2015) Aging is accompanied by a blunted muscle protein synthetic response to protein ingestion. *PLoS ONE* **10**, e0140903.
31. Yoshikawa TT & High KP (2001) Nutritional strategies to boost immunity and prevent infection in elderly individuals. *Clin Infect Dis* **33**, 1892–1900.
32. Maggini S, Pierre A & Calder PC (2018) Immune function and micronutrient requirements change over the life course. *Nutrients* **10**, E1531.
33. Watson J, Lee M & Garcia-Casal MN (2018) Consequences of inadequate intakes of vitamin A, vitamin B12, vitamin D, calcium, iron, and folate in older persons. *Curr Geriatr Rep* **7**, 103–113.
34. 2015-2020 Dietary Guidelines- health.gov [Internet]. [cited 2019 Mar 1]. Available from: https://health.gov/dietaryguidelines/2015/guidelines/
35. Advances in Nutrition Therapy Research and Application: 2011 Edition: ScholarlyBrief. Atlanta, GA: ScholarlyEditions; 2012. 53 p.
36. Abdullah Sani N & Siow ON (2014) Knowledge, attitudes and practices of food handlers on food safety in food service operations at the Universiti Kebangsaan Malaysia. *Food Control* **37**, 210–217.
37. Anderson AL, Netterville LL & Sahyoun NR (2014) 'Food safety on the go': a course for home-delivered meal programs. *J Nutr Educ Behav* **46**, 148–150.
38. Thomas KS, Gadbois EA, Shield RR *et al.* (2018) Dosa DM. 'It's not just a simple meal. it's so much more': interactions between meals on wheels clients and drivers. *J Appl Gerontol* Dec 20:733464818820226. [Epub ahead of print]https://doi.org/10.1177/0733464818820226.
39. Timonen V & O'Dwyer C (2010) 'It is nice to see someone coming in': exploring the social objectives of Meals-on-Wheels. *Can J Aging* **29**, 399–410.

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DIET AND MENTAL HEALTH

Dietary acid load in relation to depression and anxiety in adults

Alireza Milajerdi,[1,2] Ammar Hassanzadeh Keshteli,[3,4] Fahimeh Haghighatdoost,[5] Leila Azadbakht,[1,5,6] Ahmad Esmaillzadeh[1,5,6] & Peyman Adibi[4]

[1]Department of Community Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences, Tehran, Iran
[2]Students' Scientific Research Center (SSRC), Tehran University of Medical Sciences (TUMS), Tehran, Iran
[3]Department of Medicine, University of Alberta, Edmonton, Alberta, Canada
[4]Integrative Functional Gastroenterology Research Center, Isfahan University of Medical Sciences, Isfahan, Iran
[5]Food Security Research Center and Department of Community Nutrition, School of Nutrition and Food Science, Isfahan University of Medical Sciences, Isfahan, Iran
[6]Diabetes Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

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Correspondence
A. Esmaillzadeh, Department of Community Nutrition, School of Nutrition and Food Science, Isfahan University of Medical Sciences, PO Box 81745, Isfahan, Iran.
Tel.: +98 311 7922791
Fax: +98 311 6682509
E-mail: esmaillzadeh@hlth.mui.ac.ir

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Abstract

Background: No previous study has examined the association of dietary acid load (DAL) with depression and anxiety in adults. The present study aimed to investigate the association between DAL and the risk of depression and anxiety in Iranian adults.
Methods: In total, 4378 non-academic healthy personnel (1909 men and 2469 women) were included in this cross-sectional study. A validated detailed food frequency questionnaire (FFQ) was used to assess dietary intakes of participants. DAL was estimated using the protein to potassium ratio (Pro:K). Depression and anxiety were screened using an Iranian validated Hospital Anxiety and Depression Scale questionnaire.
Results: Participants with the highest DAL had a higher risk of depression compared to those in the lowest category [odds ratio (OR) = 1.57; 95% confidence interval (CI) = 1.27–1.95, $P_{trend} < 0.001$), which remained unchanged after controlling for probable confounders, such that those in the top category of DAL had a 100% higher risk of having depression than those in the bottom category (OR = 2.00; 95% CI = 1.52–2.64). In addition, a significant positive association was seen between DAL and anxiety in a crude model (OR = 1.35; 95% CI = 1.02–1.78, $P_{trend} = 0.01$) and even after adjustment for a wide range of confounders, such that participants in the top category of DAL had a 92% greater risk of anxiety than those in the bottom category (OR = 1.92; 95% CI = 1.35–2.74, $P_{trend} < 0.001$).
Conclusions: In the present study, we found a significant direct association between DAL and the risk of depression, as well as anxiety. Further studies, in particular prospective cohorts are required to confirm these findings.

Introduction

Depression and anxiety are the most prevalent mental disorders worldwide [1,2]. The prevalence of these two conditions is increasing continuously [1–3]. It is projected that depressive disorders will be the second leading cause of disease burdens in 2020 [4]. In Iran, the prevalence of anxiety and severe depressive symptoms in adults have been estimated at 29.5% and 10.39%, respectively [5].

Along with several strategies suggested to prevent mental disorders [6], diet appears to play a key role [7].

Adherence to a healthy diet, including high intakes of fish, vegetables, fruit and whole grains, was associated with a reduced risk of psychological disorders [8]. The consumption of alkaloid food items, including fruit and vegetables, was inversely linked with depression and anxiety [9], whereas the consumption of acidic foods, including red or processed meats, was positively associated with these conditions [10]. However, some studies did not find a significant association between the consumption of these food items and the risk of psychological disorders [11]. Although no previous study has investigated the association of dietary acid load (DAL) with the risk of depression and anxiety in adults, a recent study in this regard indicated that children with higher DAL had more emotional problems and hyperactivity than those with lower DAL. However, no significant associations were revealed between DAL and the risk of depression and anxiety in adolescents [12]. In addition, despite several studies linking adherence to healthy dietary patterns (which are mainly low in DAL) with a reduced risk of psychological disorders [11,13,14], other studies did not report such an association [15].

To the best of our knowledge, no previous study has examined the association of DAL with depression and anxiety in adults. As a result of the controversies noted above regarding studies on the association of acidic and alkaloid food items with depression and anxiety, further studies are required to reach a firm conclusion in this regard. The results obtained will be more important for individuals residing in the Middle East countries, where people consume less fruit and vegetables and higher amounts of refined grains, including white rice and bread [16]. Given these reasons, the present study aimed to investigate the association of DAL with depression and anxiety in a large sample of Iranian adults.

Materials and methods

Study population

The present study was conducted in the frame of the SEPAHAN (Studying the Epidemiology of Psycho-Alimentary Health and Nutrition) project, which is a cross-sectional study of non-academic healthy personnel in Isfahan province, Iran. Participants were apparently healthy adults. Detailed information about the SEPAHAN study, as well as its aims and objectives, are provided elsewhere [17]. The final data in this project were collected using self-administered questionnaires, fulfilled at two separate phases between April 2010 and May 2010. In the first phase, participants were educated how to complete the questionnaires. Data on demographic variables, as well as dietary habits, were obtained in this first phase. In the second phase, required information on psychological health was obtained. The response rate was 86% and 64% in the first and second phases, respectively. General characteristics were not significantly different between responders and nonresponders. We then merged data from these two phases, meaning that complete information was available for 4763 participants. Subjects who had missing data on any of the relevant variables including depression and anxiety ($n = 385$) were not included in the analysis. Therefore, final data for 4378 persons (1909 men and 2469 women) remained for the present study. The study was approved by the Bioethics Committee of Isfahan University of Medical Sciences, Isfahan, Iran (#189069, #189082 and #189086).

Assessment of exposure

The usual dietary intakes of participants during the past year were assessed using a validated Willett-format self-administrated 168-item semi-quantitative Food Frequency Questionnaire (FFQ). Detailed information about this questionnaire, as well as its design, food items and validity, are provided elsewhere [18,19]. In brief, the questionnaire consisted of 168 food items organised by the standard portion sizes commonly used in Iran. The questionnaire included five categories: (i) mixed dishes, including cooked or canned foods ($n = 29$); (ii) potatoes and grain-based foods ($n = 10$); (iii) dairy products, including milk and other dairy foods (e.g. butter and cream) ($n = 9$); (iv) fruit and vegetables ($n = 22$); and (v) miscellaneous foods and beverages, such as sweets, fast foods, prepared meals, nuts, desserts and beverages ($n = 36$). Participants were asked to report their daily dietary intakes based on nine multiple-choice frequency categories, including 'never or less than once a month' to '12 or more times per day.' The frequency response categories for each items varied from 6 to 9. Therefore, daily intakes of each food item were estimated and then converted to grams per day using household measures [20]. In addition, daily intakes of total energy and nutrients were obtained for each participant using the US Department of Agriculture food consumption database modified for Iranian foods. DAL was estimated using the protein to potassium ratio (Pro:K) [21].

Assessment of psychological health

The presence of depression and anxiety symptoms in participants was explored using an Iranian validated Hospital Anxiety and Depression Scale (HADS) questionnaire [22]. The HADS is useful, easy to complete and brief (14 items) tool that assesses of presence and severity of psychological disorders, as well as depression and anxiety. Each question in this questionnaire includes a four-point scale. Higher

scores indicate the increment in anxiety and depression severity, with a maximum score of 21. We considered scores between 0 and 7 in either subscale (depression and anxiety) as 'normal' and scores of ≥8 or more as indicating a psychological disorder [23]. The validity and reliability of the Persian version of HADS questionnaire was examined and approved among 167 Iranian adults by measuring the correlation between each item with its predicted scale. Pearson correlation coefficients for each item with its hypothesised scale were between 0.47 and 0.83 ($P < 0.001$) for anxiety and between 0.48 and 0.86 ($P < 0.001$) for depression, respectively [22].

Assessment of other variables

Demographic data and data on medical history of participants were obtained using questionnaires. The information obtained from each participants comprised: age, sex, marital status, smoking, presence of hyperlipidaemia, hypertension, gallstone, Crohn's disease, diabetes, cancers, stroke, myocardial infarction, heart failure, colitis, asthma and medication use including antidepressant use (fluoxetine, fluvoxamine, citalopram, sertraline, nortriptyline or amitriptyline, and imipramine) and supplement use (vitamins and minerals). The socio-economic status (SES) of participants was examined by use of the variables: family size (≤4, >4 persons), education status (academic or non-academic) and house ownership (yes/no). A score of 1 was given to subjects in the case of having ≤4 family members, academic education and house ownership. If they had >4 family members, non-academic education or were not house owners, a score of 0 was given. Finally, these scores were summed up and the SES score of 0 (poor), 1 (middle class) and 2 (high) was obtained. Physical activity of participants was assessed using the General Practice Physical Activity Questionnaire [24]. As a result of previous evidence indicating a significant reduction in the risk of chronic diseases after even 1 h of walking per week [25], participants were classified as: physically active (≥1 h week^{-1}) and inactive (<1 h week^{-1}). Anthropometric measures, including weight, height and waist circumference, were also assessed using a validated self-administered questionnaire [26]. Body mass index (BMI) was calculated as weight in kilograms divided by height in metres squared (kg m^{-2}).

Statistical analysis

Participants were categorised into quartiles based on their DAL. General characteristics and age-, sex- and energy-adjusted dietary intakes of participants across quartiles of DAL were examined using one-way analysis of variance for continuous variables and chi-squared for categorical variables. The association of DAL with the risk of depression and anxiety was assessed using logistic regression in different models. Age (continuous), sex (male/female) and energy intake (kcal day^{-1}) were adjusted for in the first model. Additional controlling for marital status (yes/no), SES (poor/middle/high), smoking (yes/no), presence of chronic conditions (yes/no), physical activity (continues), supplement use (yes/no) and antidepressant use (yes/no) was carried out in the second model. Further adjustment was performed for BMI (continuous) and dietary intake of omega-3 fatty acids (continuous) in the third model. Statistical analyses were carried out using SPSS, version 18 (SPSS Inc., Chicago, IL, USA). $P < 0.05$ was considered statistically significant.

Results

Overall, 28.6% ($n = 943$) of study participants suffered from depression or were at the borderline level and 13.6% ($n = 448$) of them had anxiety or were of borderline status. The general characteristics of participants across quartiles of DAL are presented in Table 1. Participants with a higher DAL were younger and had a lower BMI than those with lower a DAL. Compared to those in the bottom quartile, a greater percentage of participants in the top quartile of DAL were male, less likely to suffer from obesity and dietary supplement users. No significant difference was seen in the distribution of participants in terms of marital status, SES, smoking, presence of chronic conditions, physical activity and antidepressant use across quartiles of DAL.

Dietary intakes of study participants across quartiles of DAL are indicated in Table 2. High DAL was associated with higher intakes of proteins, fats, zinc, selenium, red meat, refined grains and fish, as well as lower intakes of carbohydrates, dietary fibres, whole grains, fruits, vegetables, dairies, nuts, legumes and soy ($P < 0.001$ for all). No significant difference was seen in total energy intake and the consumption of omega-3 fatty acids across quartiles of DAL.

The multivariable-adjusted odds ratios (ORs) and 95% confidence interval (CIs) for depression and anxiety across quartiles of DAL are presented in Table 3. Participants with the highest DAL had a higher risk of depression compared to those in the lowest category (OR = 1.57; 95% CI = 1.27–1.95, $P_{trend} < 0.001$). After controlling for age, sex and energy intake and other potential confounders, the association remained significant ($P < 0.001$). Even after further adjustment for BMI and dietary intakes of omega-3 fatty acids, the association was significant ($P < 0.001$), such that those in the top category of DAL had a 100% higher risk of having depression than those in the bottom category (OR = 2.00;

Table 1 General characteristics of the study population across categories of dietary acid load*

	Dietary acid load				
	Q1	Q2	Q3	Q4	$P^{\dagger}$
Age (years)	37.10 (8.07)	36.01 (7.72)	36.23 (7.94)	35.84 (7.69)	0.01
BMI (kg m^{-2})	25.27 (3.81)	24.66 (3.82)	24.82 (3.78)	24.84 (3.85)	0.01
Females (%)	65.6	62.7	57.3	47.5	<0.001
Married (%)	81.2	81.7	84.1	79.8	0.13
Obesity ‡ (%)	50.3	42.7	45.1	46.4	0.02
SES (%)					
Poor	34.9	30.6	34.7	33.5	0.49
Medium	48.7	50.7	46.9	47.4	
High	16.4	18.6	18.5	19.2	
Current smoker (%)	13.8	12.4	13.9	15.1	0.58
Chronic conditions§ (%)	4.4	3.9	5.4	4.9	0.54
Physically active¶ (%)	12.6	12.8	12.5	14.8	0.47
Supplement use†† (%)	33.0	31.7	30.1	25.2	0.003
Antidepressant use‡‡ (%)	6.9	5.2	4.6	5.5	0.21

BMI, body mass index;SES, socio-economic status.
*All data are the mean (SD) unless indicated.
†Obtained using one-way analysis of variance for continuous variables and the chi-squared test for categorical variables.
‡Obesity was defined as BMI ≥25 kg m^{-2}.
§Hyperlipidaemia, hypertension, gallstone, Crohn's disease, diabetes, cancers, stroke, myocardial infarction, heart failure, colitis, asthma.
¶Participants with physical activity of ≥1 h per week were considered as physically active.
††Supplements of vitamins and minerals.
‡‡Fluoxetine, fluvoxamine, citalopram, sertraline, nortriptyline or amitriptyline, imipramine.

Table 2 Dietary intakes of selected nutrients and food groups of study participants across categories of dietary acid load*

	Dietary acid load				
	Q1	Q2	Q3	Q4	$P^{\dagger}$
Energy (kcal day^{-1})	2362.60 (28.4)1	2371.01 (28.53)	2380.75 (27.33)	2400.96 (29.67)	0.80
Proteins (% of energy)	13.57 (0.07)	14.68 (0.06)	15.26 (0.06)	15.89 (0.09)	<0.001
Fats (% of energy)	35.93 (0.20)	37.76 (0.19)	38.58 (0.20)	38.03 (0.27)	<0.001
Carbohydrates (% of energy)	52.94 (0.24)	49.19 (0.21)	47.37 (0.23)	46.63 (0.32)	<0.001
Dietary fibre (g day^{-1})	25.49 (0.34)	23.32 (0.32)	21.65 (0.30)	19.56 (0.31)	<0.001
Omega-3 fatty acids (g day^{-1})	1.70 (0.03)	1.72 (0.03)	1.75 (0.03)	1.80 (0.03)	0.13
Zinc (mg day^{-1})	10.46 (0.13)	11.17 (0.13)	11.40 (0.13)	11.16 (0.13)	<0.001
Selenium (mg day^{-1})	88.79 (1.33)	104.24 (1.54)	111.46 (1.57)	125.14 (1.89)	<0.001
Red meat (g day^{-1})	68.85 (1.50)	80.09 (1.56)	85.59 (1.68)	80.37 (1.85)	<0.001
Whole grains (g day^{-1})	41.08 (2.38)	48.59 (3.06)	46.09 (2.83)	33.58 (2.25)	<0.001
Refined grains (g day^{-1})	306.07 (5.50)	377.29 (6.56)	402.14 (6.84)	477.02 (9.13)	<0.001
Fruits (g day^{-1})	516.61 (10.59)	334.07 (6.36)	250.97 (5.36)	162.12 (4.19)	<0.001
Vegetables (g day^{-1})	302.34 (5.80)	252.43 (4.29)	219.60 (3.23)	176.47 (3.02)	<0.001
Dairies (g day^{-1})	421.02 (11.73)	375.94 (9.09)	345.95 (8.55)	246.45 (6.45)	<0.001
Fish (g day^{-1})	11.30 (0.44)	13.02 (0.47)	14.85 (0.54)	17.04 (0.86)	<0.001
Nuts, legume and nuts (g day^{-1})	41.81 (1.44)	43.32 (1.49)	38.53 (1.32)	35.32 (1.21)	<0.001

*All values are the mean (SE); energy intake is adjusted for age and sex, all other values are adjusted for age, sex and energy intake.
†Obtained from analysis of covariance.

95% CI = 1.52–2.64). Regarding the association with anxiety, a significant positive association was seen between DAL and anxiety in a crude model (OR = 1.35; 95% CI = 1.02–1.78, P_{trend} = 0.01). After taking potential confounders (including demographic, socio-economic status and medical history, as well as physical activity and energy intake) into account, the association remained significant (OR = 1.81; 95% CI = 1.29–2.54, P_{trend} < 0.001).

This also remained unchanged when we further adjusted the analyses for BMI and dietary intakes of omega-3 fatty acids, such that participants in the top category of DAL had a 92% greater risk of anxiety than those in the bottom category (OR = 1.92; 95% CI = 1.35–2.74, $P_{trend} < 0.001$).

Discussion

The present study reports a significant direct association between DAL and the risk of depression and anxiety. These associations remained unchanged after adjustment for a wide range of confounding factors. To the best of our knowledge, no previous study has been conducted in this regard in an adult population and the present study is the first to examine such an association in an understudied population of the Middle East.

We found a direct association between DAL and the risk of depression in the present study. Although no previous study was performed investigating total DAL in relation to mental health in adults, several previous studies have reported a significant inverse association between the consumption of individual alkaloid food items and the risk of depression [27]. In addition, the consumption of acidic food items has been associated with an elevated risk of psychological disorders, including depression [28]. However, some other studies did not find a significant association between consumption of these food items and the risk of depression [15]. In addition, there are also studies in which no association was found between the diet of participants and the risk of depression or anxiety [15]. Furthermore, the findings from a large scale cross-sectional study in Netherland showed a lower plasma concentration of uric acid in patients with active depression and anxiety [29]. It was suggested that the antioxidant properties of uric acid, and not its acidic properties, might be beneficial in protection from mental disorders.

In the present study, we used the Pro:K ratio as the indicator of DAL. Adherence to a high-protein/low-fat diet has been associated with a lower risk of depression in apparently healthy adults [30]. However, it is not clear that the dietary protein in that previous study was derived from either animal or herbal sources. The findings from a cohort study showed that adherence to a high protein diet might have a protective effect on depression among men but a deleterious effect among women [31]. It was suggested that these different effects might be a result of differences in the sources of dietary proteins. Based on current knowledge, it is suggested that a higher consumption of proteins from animal sources, unlike herbal proteins, is a leading cause of psychological disorders, including depression [32]. In addition, previous studies have shown a significant inverse association between dietary potassium intake and the risk of depression [33].

We found a direct association between DAL and the risk of anxiety in the present study. Similar to depression, no previous study has been published regarding the association of DAL with anxiety. Several previous studies have found a direct significant association between the consumption of acidic food items and the risk of anxiety [34] and an inverse association for alkaloid foods [35].

Table 3 Multivariate-adjusted odds ratios and 95% confidence intervals for depression and anxiety across categories of dietary acid load*

	Dietary acid load				
	Q1	Q2	Q3	Q4	$P^{\dagger}$
Depression					
Crude	1.00	1.13 (0.90–1.41)	1.44 (1.16–1.80)	1.57 (1.27–1.95)	<0.001
Model 1	1.00	1.15 (0.91–1.46)	1.51 (1.19–1.91)	1.79 (1.41–2.26)	<0.001
Model 2	1.00	1.23 (0.94–1.61)	1.62 (1.24–2.13)	2.01 (1.54–2.63)	<0.001
Model 3	1.00	1.26 (0.96–1.66)	1.61 (1.22–2.12)	2.00 (1.52–2.64)	<0.001
Anxiety					
Crude	1.00	0.94 (0.70–1.27)	1.17 (0.88–1.56)	1.35 (1.02–1.78)	0.12
Model 1	1.00	0.87 (0.64–1.20)	1.20 (0.89–1.63)	1.44 (1.07–1.94)	0.003
Model 2	1.00	0.92 (0.64–1.33)	1.38 (0.97–1.96)	1.81 (1.29–2.54)	<0.001
Model 3	1.00	0.99 (0.68–1.45)	1.46 (1.01–2.10)	1.92 (1.35–2.74)	<0.001

Model 1: adjusted for age, sex, and energy intake. Model 2: further adjusted for marriage status; socio-economic status, smoking, presence of chronic conditions, physical activity, supplement use and antidepressants use. Model 3: further adjusted for body mass index and dietary intake of omega-3 fatty acids.

*Participants with the score of eight or more in the Hospital Anxiety and Depression Scale questionnaire were considered to have depression or anxiety.

†The *P* for trend across increasing categories of dietary acid load was calculated using multivariable logistic regression by considering the categories as ordinal variables.

However, as a result of the limited numbers of studies conducted in this regard, further studies are needed to reach a firm conclusion.

Although, an explanation of the exact mechanisms by which DAL may influence risk of depression and anxiety is lacking, there are some intermediary pathways via which metabolic acidosis may promote psychological disorders. For example, the interaction of dietary proteins with some polymorphisms might influence mental function [30]. It should be noted that acidic diets are typically rich in animal and processed proteins and low in fruit and vegetables [36]. Animal foods and process meats are rich in saturated and trans fatty acids [37], whereas fruit and vegetables have large amounts of flavonoids and antioxidants along with different vitamins and minerals [38]. A higher consumption of saturated and trans fatty acids has been associated with greater mental and physiological stress, which might be a result of the increased oxidative stress [39]. Otherwise, an adherence to diets rich in fruit and vegetables with high amounts of antioxidant nutrients, including vitamin A and potassium, has been linked to the lowered risk of psychological disorders [40].

The present study is the first to investigate the association of DAL with the risk of depression and anxiety in adults. As strengths, the present study had a large sample size in which we adjusted the analysis for a wide range of potential confounders, including dietary and nondietary covariates. In addition, the study was conducted in a developing country, where limited information is available about diet–disease associations. However, some limitations should also be noted. As a result of the observational design of the study, it was impossible to confer causality. In addition, DAL was estimated using a nutrient-based method, which may make it a potential source of bias. Furthermore, depression and anxiety were examined based on a self-reported questionnaire, which may lead to the misclassification of study participants. Moreover, as a result of the use of a FFQ, misclassification of study participants in terms of dietary intakes cannot be excluded. Finally, the study was conducted on a population from Isfahan province and so caution is warrantedtaken when generalising the findings to the entire Iranian adult population.

In conclusion, we found a significant direct association between DAL and the risk of depression, as well as anxiety, in the current study. Further studies, in particular those of a prospective design, are required to confirm these findings.

Transparency declaration

The lead author affirms that this manuscript is an honest, accurate and transparent account of the study being reported. The lead author affirms that no important aspects of the study have been omitted and that any discrepancies from the study as planned have been explained.

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Conflict of interests, source of funding and authorship

The authors declare that they have no conflicts of interest.
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AM wrote the manuscript. AM and AE analysed and interpreted the data. AHK, FH, LA, AE, and PA designed the study. AM and AE revised the manuscript.

References

1. Ferrari A, Somerville A, Baxter A *et al.* (2013) Global variation in the prevalence and incidence of major depressive disorder: a systematic review of the epidemiological literature. *Psychol Med* **43**, 471–481.
2. Baxter A, Scott K, Vos T *et al.* (2013) Global prevalence of anxiety disorders: a systematic review and meta-regression. *Psychol Med* **43**, 897–910.
3. Devries KM, Mak JY, Bacchus LJ *et al.* (2013) Intimate partner violence and incident depressive symptoms and suicide attempts: a systematic review of longitudinal studies. *PLoS Med* **10**, e1001439.
4. Murray CJ & Lopez AD (1997) Alternative projections of mortality and disability by cause 1990–2020: global burden of disease study. *Lancet* **349**, 1498–1504.
5. Noorbala AA, Faghihzadeh S, Kamali K *et al.* (2017) Mental health survey of the Iranian Adult population in 2015. *Arch Iran Med* **20**, 128–134.
6. Keyes CL (2007) Promoting and protecting mental health as flourishing: a complementary strategy for improving national mental health. *Am Psychol* **62**, 95.
7. Lakhan SE & Vieira KF (2008) Nutritional therapies for mental disorders. *Nutr J* **7**, 2.
8. Quirk SE, Williams LJ, O'Neil A *et al.* (2013) The association between diet quality, dietary patterns and

depression in adults: a systematic review. *BMC Psychiatry* **13**, 175.
9. Saghafian F, Malmir H, Saneei P *et al.* (2018) Fruit and vegetable consumption and risk of depression: accumulative evidence from an updated systematic review and meta-analysis of epidemiological studies. *Br J Nutr* **119**, 1087–1101.
10. Rahmani J, Milajerdi A & Dorosty-Motlagh A (2018) Association of the Alternative Healthy Eating Index (AHEI-2010) with depression, stress and anxiety among Iranian military personnel. *J R Army Med Corps* **164**, 87–91.
11. Wu S, Fisher-Hoch SP, Reininger BM *et al.* (2018) Association between fruit and vegetable intake and symptoms of mental health conditions in Mexican Americans. *Health Psychol* **37**, 1059.
12. Buhlmeier J, Harris C, Koletzko S *et al.* (2018) Dietary acid load and mental health outcomes in children and adolescents: results from the GINIplus and LISA birth cohort studies. *Nutrients* **10**, E582.
13. Poorrezaeian M, Siassi F, Milajerdi A *et al.* (2017) Depression is related to dietary diversity score in women: a cross-sectional study from a developing country. *Ann Gen Psychiatry* **16**, 39.
14. Milajerdi A, Keshteli AH, Afshar H *et al.* (2018) Dietary total antioxidant capacity in relation to depression and anxiety in Iranian adults. *Nutrition* **65**, 85–90.
15. Jans G, Matthys C, Bogaerts A *et al.* (2017) Depression and anxiety: lack of associations with an inadequate diet in a sample of pregnant women with a history of bariatric surgery – a multicenter prospective controlled cohort study. *Obes Surg* **28**, 1629–1635.
16. Esmaillzadeh A, Boroujeni HK & Azadbakht L (2012) Consumption of energy-dense diets in relation to cardiometabolic abnormalities among Iranian women. *Public Health Nutr* **15**, 868–875.
17. Adibi P, Keshteli AH, Esmaillzadeh A *et al.* (2012) The study on the epidemiology of psychological, alimentary health and nutrition (SEPAHAN): overview of methodology. *J Res Med Sci* **17**, S292–S298.
18. Azadbakht L, Mirmiran P, Esmaillzadeh A *et al.* (2005) Dairy consumption is inversely associated with the prevalence of the metabolic syndrome in Tehranian adults. *Am J Clin Nutr* **82**, 523–530.
19. Mirmiran P, Esmaillzadeh A & Azizi F (2005) Dairy consumption and body mass index: an inverse relationship. *Int J Obes* **29**, 115.
20. Ghaffarpour M, Houshiar-Rad A & Kianfar H (1999) The manual for household measures, cooking yields factors and edible portion of foods. *Tehran Nashre Olume Keshavarzy* **7**, 213.
21. Frassetto LA, Todd KM, Morris R *et al.* (1998) Estimation of net endogenous noncarbonic acid production in humans from diet potassium and protein contents. *Am J Clin Nutr* **68**, 576–583.
22. Montazeri A, Vahdaninia M, Ebrahimi M *et al.* (2003) The Hospital Anxiety and Depression Scale (HADS): translation and validation study of the Iranian version. *Health Qual Life Outcomes* **1**, 14.
23. Zigmond AS & Snaith RP (1983) The hospital anxiety and depression scale. *Acta Psychiatr Scand* **67**, 361–370.
24. Policy PA. Health Improvement Directorate(2009) *The General Practice Physical Activity Questionnaire (GPPAQ) A Screening Tool to Assess Adult Physical Activity Levels, within Primary Care*. London: Department of Health.
25. Oguma Y & Shinoda-Tagawa T (2004) Physical activity decreases cardiovascular disease risk in women: review and meta-analysis. *Am J Prev Med* **26**, 407–418.
26. Aminianfar S, Saneei P, Nouri M *et al.* (2015) Validation study of self-reported anthropometric indices among the staff of the Isfahan University of Medical Sciences, Isfahan, Iran. *J Isfahan Med School* **33**, 1318–1327.
27. Saghafian F, Malmir H, Saneei P *et al.* (2018) Consumption of fruit and vegetables in relation with psychological disorders in Iranian adults. *Eur J Nutr* **57**, 2295–2306.
28. Jacka FN, Pasco JA, Mykletun A *et al.* (2010) Association of Western and traditional diets with depression and anxiety in women. *Am J Psychiatry* **167**, 305–311.
29. Black CN, Bot M, Scheffer PG *et al.* (2018) Uric acid in major depressive and anxiety disorders. *J Affect Disord* **225**, 684–690.
30. Pooyan S, Rahimi MH, Mollahosseini M *et al.* (2018) A high-protein/low-fat diet may interact with vitamin D-binding protein gene variants to moderate the risk of depression in apparently healthy adults. *Lifestyle Genom* **11**, 64–72.
31. Wolfe AR, Arroyo C, Tedders SH *et al.* (2011) Dietary protein and protein-rich food in relation to severely depressed mood: a 10 year follow-up of a national cohort. *Prog Neuropsychopharmacol Biol Psychiatry* **35**, 232–238.
32. Hosseinzadeh M, Vafa M, Esmaillzadeh A *et al.* (2016) Empirically derived dietary patterns in relation to psychological disorders. *Public Health Nutr* **19**, 204–217.
33. Kim T-H, Choi J-Y, Lee H-H *et al.* (2015) Associations between dietary pattern and depression in Korean adolescent girls. *J Pediatr Adolesc Gynecol* **28**, 533–537.
34. Jacka FN, Pasco JA, Williams LJ *et al.* (2012) Red meat consumption and mood and anxiety disorders. *Psychother Psychosom* **81**, 196–198.
35. Nguyen B, Ding D & Mihrshahi S (2017) Fruit and vegetable consumption and psychological distress: cross-sectional and longitudinal analyses based on a large Australian sample. *BMJ Open* **7**, e014201.

36. Passey C (2017) Reducing the dietary acid load: How a more alkaline diet benefits patients with chronic kidney disease. *J Ren Nutr* **27**, 151–160.
37. Valsta L, Tapanainen H & Männistö S (2005) Meat fats in nutrition. *Meat Sci* **70**, 525–530.
38. Van Duyn MAS & Pivonka E (2000) Overview of the health benefits of fruit and vegetable consumption for the dietetics professional: selected literature. *J Am Diet Assoc* **100**, 1511–1521.
39. Chang M-W, Brown R & Nitzke S (2016) Fast food intake in relation to employment status, stress, depression, and dietary behaviors in low-income overweight and obese pregnant women. *Matern Child Health J* **20**, 1506–1517.
40. Sánchez-Villegas A, Pérez-Cornago A, Zazpe I *et al.* (2018) Micronutrient intake adequacy and depression risk in the SUN cohort study. *Eur J Nutr* **57**, 2409–2419.

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DIET AND MENTAL HEALTH

Effect of probiotic and prebiotic versus placebo on appetite in patients with major depressive disorder: *post hoc* analysis of a randomised clinical trial

A. Kazemi,[1] A. A. Noorbala[2] & K. Djafarian[3]

[1]Nutrition Research Center, Shiraz University of Medical Sciences, Shiraz, Iran
[2]Psychosomatic Medicine Research Center, Imam Khomeini Hospital, Tehran University of Medical Sciences, Tehran, Iran
[3]Department of Clinical Nutrition, School of Nutritional Sciences and Dietetic, Tehran University of Medical Sciences, Tehran, Iran

Keywords
appetite, leptin, major depressive disorders, prebiotic, probiotic.

Correspondence
K. Djafarian, Tehran University of Medical Sciences, No 44, Hojjat-dost Alley, Naderi Street, Keshavarz Boulevard, Tehran, 14166/43931, Iran.
Tel.: +98 912 6654577
Fax: +98 (0) 21 88974462
E-mail: kdjafarian@tums.ac.ir

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Abstract

Background: Poor appetite and weight loss are common in melancholic depression. Probiotics and prebiotics have the capacity to affect host behaviour, appetite and weight change by modulating the gut microbiome. The aim of this *post hoc* analysis was to investigate the effect of supplementation with probiotic and prebiotic on appetite, in parallel with body mass index (BMI), weight and energy intake, in patients with major depressive disorder (MDD).

Methods: We extracted data from a clinical trial with 81 patients. The participants were randomly assigned to receive probiotic (*Lactobacillus helveticus* and *Bifidobacterium longum*), prebiotic (galactooligosaccharide) or placebo for 8 weeks. Appetite, weight, BMI, dietary intake, serum leptin and physical activity were measured. Subjective appetite rating was evaluated every 2 weeks using visual analogue scales (VAS) to assess satiety, hunger, fullness and desire to eat. Serum leptin was measured by an enzyme-linked immunosorbent assay. Physical activity was measured using the international physical activity questionnaire. A repeated measures analysis of variance model was used to analyse VAS data and analysis of variance/analysis of covariance models for dietary intake, BMI, weight and leptin data.

Results: VAS data analyses indicated no significant intervention–time interactions but did show a significant increase over time for desire to eat within the probiotic group ($P = 0.025$). No significant difference in either BMI or weight was seen among the groups. Energy intake and leptin were significantly increased in the probiotic group compared to the prebiotic.

Conclusions: Overall, probiotic supplementation for 8 weeks among MDD patients resulted in improvement of appetite, whereas prebiotic administration had no significant effect on appetite.

Introduction

Appetite disturbance and weight problems are common in major depressive disorder (MDD). However, MDD patients exhibit marked heterogeneity in terms of both appetite and satiety. Although appetite decreases in melancholic depression [(1)], it increases in the atypical type of depression [(2)]. Other subtypes of depression are not associated with appetite disturbances or body weight changes [(1)].

In recent years, an emerging field of research has revealed the role of the gut microbiota with respect to modulating the activity of the central nervous system [(3)]. The human gut is colonised by almost 100 trillion microorganisms that can be classified either as pathogenic, neutral or beneficial for the host [(4)]. Recent evidence obtained in animals and humans has demonstrated the capacity of the gut microbiome to affect host behaviour, appetite and body weight regulation [(3)]. Multiple

mechanisms have been proposed for the effect of gut microbiota on mood. First, some of the bacteria are able to either directly synthesise the neurotransmitters that are related to the mood (serotonin, gamma-aminobutyric acid, histamine, noradrenaline and adrenaline) or indirectly increase the precursors of these neurotransmitters [5]. Second, a balanced gut microbiota prevents immune system activation and cytokine production by maintaining the epithelial barrier [6]. This is important because depression is associated with a chronic low-grade inflammatory response [7]. The inflammatory cytokine results in changes in neurotransmitter metabolism. Finally, an imbalanced gut microbiota leads to hyperactivity of the hypothalamic–pituitary–adrenal (HPA) axis indirectly as a result of inflammatory cytokines [8] and an impairment in serotonin metabolism [9]. HPA axis dysregulation has been implicated in the pathogenesis of MDD [10].

Prebiotics and probiotics can be used to manipulate the microbiota and improve mood and appetite [11]. Probiotics comprise 'live microorganisms that, when administered in adequate amounts, confer a health benefit to the host' [12]. Prebiotics are also dietary nonviable food components that can act indirectly through microbiota-dependent mechanisms [13].

The results of studies on the effect of probiotics on weight change are inconsistent and most of them do not evaluate their effect on appetite [14]. A recent study showed that probiotic supplementation could sustain weight loss in dieting women, and help curb appetite sensations [15]. The effect of probiotics on appetite in people with depression may be different and dependent on the host appetite status [1]. Most of the clinical trials that have investigated the effect of prebiotics on appetite, energy intake and weight change revealed no beneficial effect for any of these outcomes [16]. However, the majority of these studies were conducted in nondepressed individuals and the compounds that were investigated as prebiotics were inulin-type fructans, which are nondigestible, fully soluble and fermentable food ingredients with known prebiotic properties. To the best of our knowledge, no study has investigated the effect of probiotics and prebiotics on appetite in patients with depression. The present *post hoc* analysis was conducted aiming to evaluate the effect of probiotics and prebiotics on appetite in patients with MDD.

Materials and methods

Design, randomisation and blinding

The present study, designed as a 8-week, double-blind, randomised controlled trial with three parallel arms, has been reported previously (IRCT.ir: IRCT2015092924271N1). The study was registered and approved by the ethics committee of the Tehran University of Medical Sciences. We obtained written informed consent from all participants. In our initial study, we considered a duration of 8 weeks based on previous studies on the effect of probiotic on depression, which demonstrated a significant improvement [17–20] in mood status within a similar or shorter timeframe.

Patients were randomly assigned to one of the three groups (i.e. probiotic, prebiotic or placebo), identified as groups A, B or C, using permuted block randomisation with a block length of six. Based on their age, participants were stratified into two strata and assigned a treatment code using two separate randomisation lists generated by an independent statistician (www.randomization.com). Both participants and investigators were blinded to the randomisation table, the code assignments and the procedure.

Participants

Participant selection has been described previously [20]. Briefly, study participants were selected from patients who were referred to the clinic of the Bahman hospital and were included in the study if they were diagnosed with mild to moderate major depression, were aged 18–50 years and had been taking an antidepressant drug (i.e. sertraline, fluoxetine, citalopram or amitriptyline) for 3 months or more prior to the start of the trial. The severity of depression was diagnosed by a psychiatrist. Participants were not included if they had any of the following criteria: history of renal, hepatic, cardiovascular or respiratory diseases; pregnancy or lactation; regular intake of probiotics during the last 2 months before study recruitment; intake of antioxidant or omega-3 supplements 6 weeks before the start of the study; alcohol intake; cigarette smoking (more than 5 day^{-1} during the last 6 months) or tobacco use (pipe or hookah, at least one time during the last month); opiate addiction; history of heart attack or stroke; following a specific diet; participation in another study during the last 2 months. participants were also excluded if they had any significant change in their regular diet and lifestyle; any change in the drug regimen; inflammatory diseases that lasted for more than 1 week during the study; and an intake of antibiotics during the study. Participants were instructed not to consume any other probiotic supplements during the course of the trial.

Intervention

All supplements were provided by Lallemand Health Solutions (Mirabel, QC, Canada). The supplements were provided in a powder form and were packed in numerically coded sachets (5 g), each containing 10 billion

colony-forming units ($\geq 10 \times 10^9$ CFU) of freeze-dried *Lactobacillus helveticus* R0052 and *Bifidobacterium longum* R0175 (CNCM strain I-3470). The excipients used were: xylitol, maltodextrin, plum flavour and malic acid. The placebo product contained only the excipients, and the prebiotic product was composed of galactooligsaccharide and 0.2% plum flavour. The supplementation sachets were identical with respect to colour, size and taste. Participants received half the sachets at the baseline visit and the remainder at the 4-week visit. Participants were instructed to keep the sachets refrigerated and to consume one sachet at the same time daily. Participants were monitored for compliance and probable adverse events by telephone every 2 weeks. After completion of the study, the returned empty sachets were counted for assessment of compliance. Subjects were deemed compliant when they consumed at least 80% of the recommended sachets.

Procedure and secondary outcomes

The previously published clinical trial started in July 2016 and finished in April 2017 [20]. Fasting blood samples were collected between 08.00 h and 09.00 h at the beginning and end of the 8-week trial. The samples were immediately centrifuged (Universal, Germany) at 1700 *g* for 10 min to separate the serum and stored at −80 °C until analysis.

Visual analogue scales (VAS) assessing satiety, hunger, fullness and desire to eat were used to assign subjective appetite ratings as the primary outcome of the study [21–23]. Each scale was 100 mm in length with words anchored at each end, expressing the most positive and negative rating of the category (e.g. for hunger 'I am not hungry at all' at 0 mm and 'I have never felt more hungry' at 100 mm). The VAS questionnaire was completed before the lunchtime meal every 2 weeks. At each completion, subjects did not receive any information about their previous ratings.

The secondary outcomes were weight, body mass index (BMI), dietary intake, serum leptin and physical activity. Body weight and height were measured in an overnight fasting state, with minimal clothing and without shoes using a digital scale (Seca, Hamburg, Germany) at baseline and at the end of the study. BMI was calculated as weight (kg) divided by height squared (m^2). Serum leptin was measured using a commercially available enzyme-linked immunosorbent assays kit [Human leptin (highly sensitive) assay kit; IBL, Fujioka City, Japan].

Participants were requested not to change their routine physical activity or usual dietary intakes throughout the study. They were asked to record their dietary intakes for three non-consecutive days (two usual days and one weekend day) at baseline and at the end of trial. To obtain nutrient intakes of participants based on a 3-day food diary, we used Nutritionist IV software (First Databank, San Bruno, CA, USA) modified for Iranian foods. The dietary records were based on estimated values in household measurements. Physical activity was recorded using the short International Physical Activity Questionnaire at baseline and at the end of the study. Physical activity was described as metabolic equivalents (METs) in hours per day. To compute the METs for each subject, we multiplied the times (h $week^{-1}$) reported for each physical activity by its related METs coefficient in accordance with standard tables.

Statistical analysis

SPSS, version 16.0 (SPSS Inc., Chicago, IL, USA) was used to conduct the statistical analysis. $P < 0.05$ (two-sided) was considered statistically significant. Continuous variables were summarised by treatment groups as the mean (SD) and categorical variables were summarised as counts and percentages. An analysis of variance (ANOVA)/analysis of covariance (ANCOVA) model was used to compare the final values for weight, BMI, dietary intake, leptin and METs between groups after adjusting for baseline values. Bonferroni multiple comparisons were applied as a *post hoc* test to compare data between the groups in case the results were significant. Repeated measure ANOVA was used to analyse the VAS. To verify normality, a Kolmogorov–Smirnov test was used. Data transformation was performed if a variable distribution was not normal. $P < 0.05$ were considered statistically significant for all analyses. Sample size calculations, which were based on significance of the primary outcome (Beck Depression Inventory score), were published previously [20,24].

Results

Trial enrollment, patient screening, study-group assignments and follow-up summary of subjects have been reported previously [20]. Briefly, from 230 referred patients, 110 subjects (32 men and 78 women) were enrolled in the study and were randomly assigned to the probiotic group ($n = 38$), prebiotic group ($n = 36$) or placebo group ($n = 36$) (Fig. 1).

Baseline characteristics of the participants included in the intention-to-treat analyses for each study group are shown in Table 1. There was no significant difference between groups for baseline characteristics. To determine the difference in outcome variables between intervention groups, the intention-to-treat approach was used for analysis of weight and BMI, and the per-protocol approach was applied to the dietary intake, physical activity and appetite outcome variables.

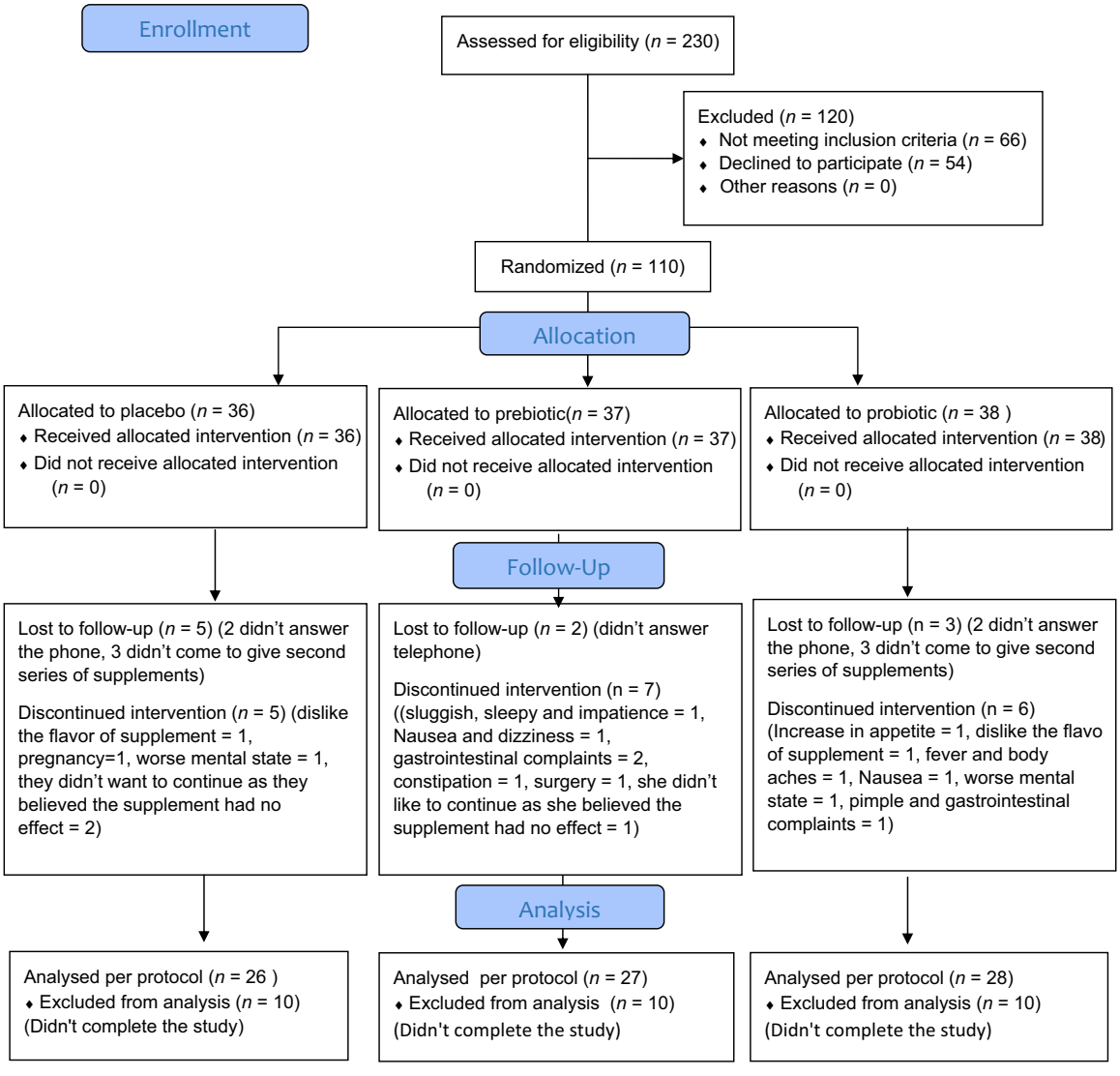

Figure 1 Summary of the patient flow diagram.

Table 1 Baseline characteristics of participating subjects

Characteristic	Probiotic (*n* = 38)	Prebiotic (*n* = 36)	Placebo (*n* = 36)
Gender, *n* (%)			
Male	11 (28.9)	9 (25)	12 (33.3)
Female	27 (71)	27(75)	24 (66.6)
Age (years), mean (SD)	36.15 (7.85)	37.35 (7.97)	36 (8.47)
BDI score	18.25 (11.4)	19.43 (13.5)	18.74 (12.8)

BDI, Beck Depression Inventory score.

Physical activity decreased in all three groups, without any significant difference in the average physical activity levels between the three groups, as well as in pairwise comparisons.

The appetite of study participants was assessed using a four-component VAS: desire to eat, hunger, satiety and fullness. Analysis of the VAS data using a repeated measures ANOVA yielded no significant intervention–time interactions but did show a significant increase over time for desire to eat within the probiotic group ($P = 0.025$) (Fig. 2a). Although an increasing trend in hunger was seen within the probiotic group, this was not statistically significant ($P = 0.13$) (Fig. 2b). Satiety and fullness did not change significantly over time in the three groups (Fig. 2c,d). ANCOVA for VAS data (adjusted for baseline) at weeks 2, 4, 6 and 8, showed that probiotic increased the desire to eat at weeks 6 and 8, at the same time as significantly increasing hunger only at week 8. Baseline values were included as covariates in the ANCOVA.

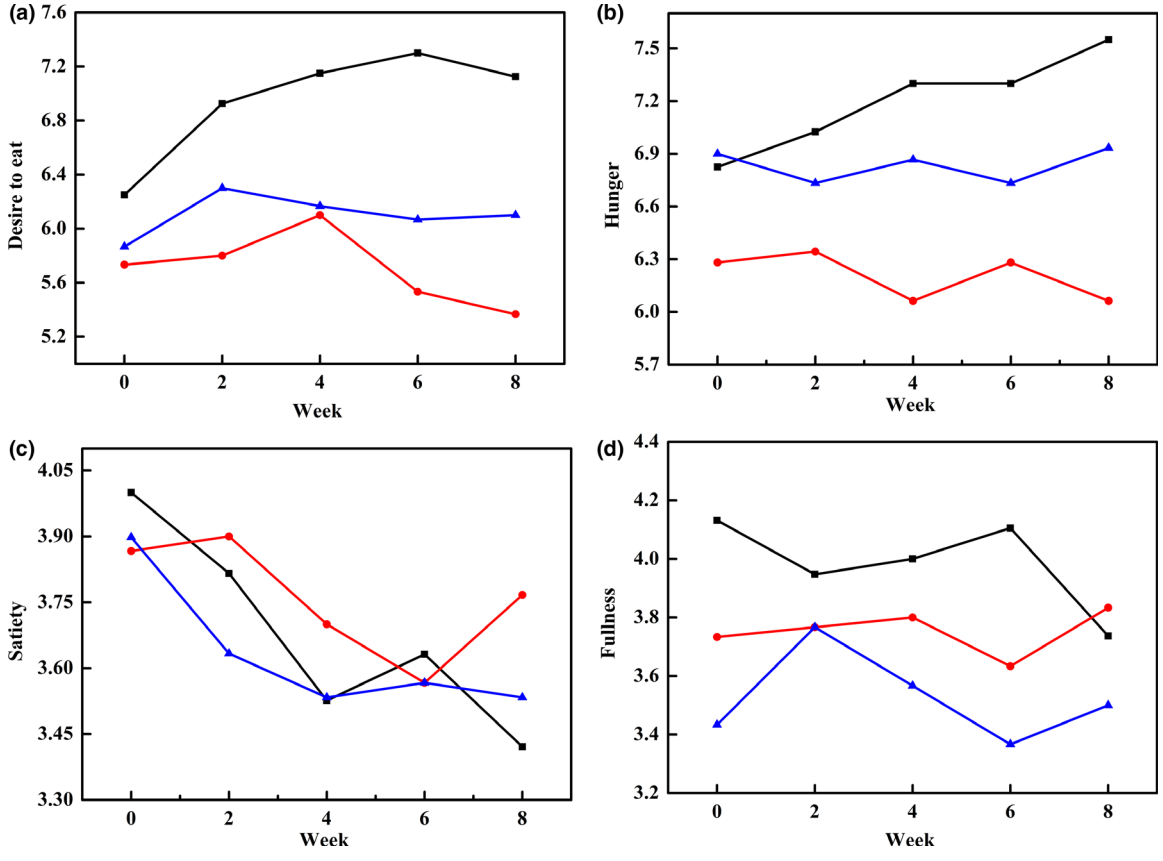

Figure 2 Mean appetite ratings at baseline, weeks 2, 4, 6 and 8, recorded on 100-mm lines, during the consumption of probiotic , probiotic —■—, prebiotic —●—, and placebo —▲—. (a) Desire to eat; (b) Hunger; (c) Satiety; (d) Fullness.

Dietary intake data are presented in Table 2. Energy intake increased in the probiotic and placebo groups, whereas it decreased in the prebiotic group. Only the difference between the probiotic and prebiotic group was significant in the pairwise comparison ($P = 0.03$, Cohen's $d = 0.48$). There was no significant difference between the three groups for macro- and micronutrient intake, except for fat ($P = 0.04$). In a pairwise comparison, total fat intake decreased in the prebiotic group compared to the probiotic ($P = 0.04$, Cohen's $d = 0.4$) and placebo ($P = 0.03$, Cohen's $d = 0.44$); however, the percentage fat from total caloric intake did not decrease significantly. Among micronutrients, only selenium was decreased in the probiotic group compared to placebo ($P = 0.02$, Cohen's $d = 0.37$).

There was no significant difference in BMI or weight among the three groups[24], nor was there a difference via pairwise comparison using ANOVA/ANCOVA tests in this analysis (Tables 3 and 4). For leptin levels, no difference was observed when comparing the three groups by ANOVA/ANCOVA tests, although pairwise comparisons revealed that serum leptin levels increased significantly in the probiotic group compared to the prebiotic (Table 4).

Discussion

According to our *post hoc* analysis of this randomised controlled trial [20] of patients with MDD, probiotic supplementation resulted in an increase in both desire to eat and hunger. Most studies investigating the effect of probiotics on weight or BMI have not evaluated appetite. The only study that has measured appetite was conducted by Sanchez *et al.* [15] who investigated the effect of probiotics together with a weight loss programme on appetite in obese subjects. In this study, probiotics led to an increase in the fasting desire to eat in women, at the same time as increasing fullness in the fasting state in men. By contrast, satiety efficiency at lunch increased in both genders[15].

It is now established that the effects of probiotics are strain-dependent [21]. We used probiotic strains [19,25,26] and a prebiotic component [27–29] that were shown to be effective at improving mood in previous studies. Similar to the other outcomes, the effect of probiotics on appetite

Table 2 Mean (SD) of dietary intake at baseline and at the end of week 8

	Probiotic		Prebiotic		Placebo		
	Baseline	End	Baseline	End	Baseline	End	*P* value
Energy (kcal)	1537 (317)	1662 (334)	1467 (409)	1405 (421)	1505 (565)	1547 (570)	0.06
Protein (g)	53.1 (17.4)	53.2 (13.7)	53.7 (19.9)	52.11 (26)	56.4 (24.1)	59.2 (24.1)	0.35
Protein (%)	13.3 (2.4)	12.6 (2.3)	14.5 (2.3)	14 (3.3)	14.9 (2.2)	14.8 (4.4)	0.12
Fat (g)	49.9 (14.6)	54.6 (19.5)	50.1 (19.7)	46 (22)	50.8 (20.9)	55.6 (24.7)	0.04
Fat (%)	28 (7.8)	29.9 (6.2)	30 (7.9)	28.9 (7.7)	30 (5.2)	32 (6.4)	0.16
CHO (g)	233.6 (56)	244 (60)	198.6 (67)	199 (57)	209 (78)	207 (82)	0.72
CHO (%)	58.4 (7.9)	58 (6.3)	55 (7.5)	56.4 (8.3)	54.8 (6.2)	52.4 (8.1)	0.22
Fibre (g)	13.4 (7)	11.8 (5.7)	10.4 (4.6)	11.6 (6.1)	11.9 (4.6)	11.2 (4.8)	0.7
Cholesterol (mg)	155.1 (96.3)	175.3 (101.6)	164.9 (115.5)	140.2 (99)	152.3 (128.6)	136 (129.4)	0.24
Mg (mg)	157 (59.3)	161.5 (46)	138.3 (43.5)	164.5 (62.5)	150.9 (68.8)	143.2 (58.4)	0.22
Zn (mg)	5 (1.7)	5.2 (2.5)	5.5 (2.1)	5 (2.7)	6 (3.4)	6.4 (3.2)	0.32
Se (μg)	0.07 (0.05)	0.06 (0.03)	0.06 (0.03)	0.07 (0.05)	0.06 (0.05)	0.08 (0.04)	0.05
Vitamin E (mg)	2.8 (2.3)	2 (2.3)	1.94 (1.89)	2.26 (1.46)	2.1 (2.96)	2.46 (3.1)	0.75
Vitamin C (mg)	44.5 (64.9)	63.5 (122)	61.4 (65.4)	81.9 (69)	53.8 (53.7)	58.3 (60.8)	0.87
MET (h week^{-1})	19.6 (17.34)	15.54 (14.15)	16.87 (12.5)	14.14 (8.16)	17.18 (13.26)	15.25 (14.41)	0.94

CHO, carbohydrate; MET, metabolic equivalents; Mg, magnesium; Se, selenium; Zn, Zinc.

Table 3 Mean (SD) values of weight, body mass index (BMI) and leptin at baseline and at the end of week 8

	Probiotic		Prebiotic		Placebo		
Outcome	Baseline	End	Baseline	End	Baseline	End	*P* value
Weight (kg)	71.7 (11.8)	72.8 (12.4)	72.5 (15.6)	72.8 (15.9)	73.3 (14.1)	73.8 (13.7)	0.27†
							0.84‡
BMI (kg m^{-2})	26.2 (4.0)	26.7 (4.4)	27 (5.1)	27.2 (5.2)	26.6 (4.9)	26.9 (4.6)	0.28†
							0.43‡
Leptin (ng mL^{-1})	4.9 (3.2)	5.6 (3.2)	6 (3.6)	5.6 (3.7)	5 (3.8)	4.9 (3.8)	0.08†
							0.07§

BMI, Body mass index.
†Adjusted for baseline values.
‡Adjusted for baseline and energy intake.
§Adjusted for baseline, energy intake and BMI.

Table 4 Pairwise comparison of the groups

	Comparisons (*P* value)					
	Probiotic versus placebo		Prebiotic versus placebo		Probiotic versus prebiotic	
Outcome	ES† *d*	*P* value	ES† *d*	*P* value	ES† *d*	*P* value
Weight (kg)	0.05	0.28†	0.03	0.88†	0.09	0.06†
		0.75‡		0.92‡		0.50‡
BMI (kg m^{-2})	0.023	0.27†	0.02	0.91†	0.04	0.053†
		0.25‡		0.74‡		0.29‡
Leptin (ng mL^{-1})	0.23	0.08†	0.07	0.91†	0.32	0.03†
		0.07§		0.71§		0.06§

BMI, body mass index; ES, effect size.
†Adjusted for baseline values.
‡Adjusted for baseline and energy intake.
§Adjusted for baseline, energy intake and BMI.

may depend on the host appetite status and the reason for impaired appetite.

To our knowledge, no study has investigated the effect of probiotics on the appetite of depressed patients. However, several mechanisms may explain the effect of probiotics on appetite in people with depression as observed in the present study. Probiotics have been shown to decrease inflammatory cytokines and modulate neurotransmitters such as serotonin [30,31], which may improve appetite in depressed subjects. Inflammatory cytokines induce anorexia by interacting with appetite-regulating neurotransmitters (inhibiting neuropeptide Y and stimulating the release of α-melanocyte-stimulating hormone in the hypothalamus) [30], as well as stimulating the release of hormones that are considered to be appetite-regulating factors, such as glucagon, insulin, leptin [30] and glucocorticoids [32]. Furthermore, inflammation induces

anhedonic responses by disrupting the basic reward behaviour [33,34]. Serotonin improves anhedonia; the reward-related areas in the brain, both cortical and subcortical, are innervated extensively by serotonergic neurones [35]. Moreover, the serotonergic transmitter system has a modulatory effect on the reward network via different receptors and the serotonin transporter [36–38]. Furthermore, the present study confirmed the results of five previous studies showing the absence of a significant effect of prebiotics (inulin-type fructans) on appetite [39–43]. Two studies, one conducted in obese subjects [44] and one in children [45], indicated a loss of appetite after inulin consumption.

The probiotic increased energy intake, whereas the prebiotic decreased it; however, these changes were not significant compared to the placebo. Most studies indicated no significant effect of probiotics on energy intake. Similarly, in a systematic review of studies that assessed the effect size of prebiotics on energy intake, 11 studies demonstrated no significant effect of prebiotics on energy intake, whereas one study revealed a reduction in energy intake by prebiotic consumption [16].

Our results revealed that probiotic supplementation increased leptin levels compared to the prebiotic. This result was unexpected considering that appetite increased in the probiotic group. The results of previous studies on the effect of probiotics on leptin are inconsistent. A study on heavy smokers indicated significant reduction of leptin following 6 weeks supplementation with *Lactobacillus plantarum* [46]. In another study, 6 months of treatment with probiotics in morbidly obese, non-alcoholic, fatty liver disease (NAFLD) patients who underwent laparoscopic sleeve gastrectomy did not significantly modulate serum leptin levels [47]. Moreover, two other studies in obese individuals demonstrated no significant effect of 2 [48] and 12 months [49] of probiotic supplements together with a low calorie diet compared to the low calorie diet alone. The only study that examined the effect of prebiotics on leptin indicated that oligofructose, as well as probiotics, decreased leptin significantly in NAFLD patients after 12 weeks [33]. The main difference between these previous studies and our study is the non-depressed obese participants versus normal to obese depressed participants in the present study. The studies investigating the effect of antidepressants on the improvement in the symptoms of depression indicated more elevated leptin values with the improvement from depression [50]. Although cortisol stimulates leptin secretion from adipocytes at the initial phases of depression, chronic stimulation causes a down-regulation in glucocorticoid receptors on adipose tissue. As antidepressants or probiotics improve the depression, glucocorticoid receptor resistance will resolve, and the sensitivity of adipocytes to the leptin-stimulating effect of glucocorticoids will be increased [51,52].

Neither the probiotic, nor the prebiotic significantly affected weight or BMI in the present study[24]. A lack of significant change in BMI despite an increase in appetite and leptin in the probiotic group may be a result of the duration of the present study, which might have not been sufficiently long enough to reveal a significant change in BMI. Previous studies investigating the effect of probiotics on weight or BMI yielded inconsistent results and a meta-analysis revealed that these effects were strain-specific [14]. Our results from the prebiotic group are consistent with five studies reporting no effect of prebiotics on weight loss in normal [53] or overweight individuals [43,54,55]. On the other hand, two studies conducted on overweight and obese subjects observed a weight-reducing effect of prebiotics [56,57].

The limitations of the present study include a relatively small sample size, the lack of faecal microbiome analysis and a short study duration. A strength of the present study is the selection of probiotic strains that have been shown to improve mood disorders in previous studies.

In conclusion, the probiotic increased the desire to eat and serum leptin levels, whereas it had no effect on the weight or BMI in patients with MDD. The probiotic may increase appetite and energy intake by improving depression, which leads to an increase in leptin levels as a compensatory mechanism. Galactooligosaccharide did not significantly change appetite, energy intake, weight or leptin levels.

Transparency declaration

The authors affirm that this manuscript is an honest, accurate and transparent account of the study being reported. The reporting of this work is compliant with CONSORT guidelines. The lead author affirms that no important aspects of the study have been omitted and that any discrepancies from the study as planned in IRCT.ir: IRCT2015092924271N1 have been explained.

Conflict of interests, source of finding and authorship

The authors declare that they have no conflicts of interest.

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AK was responsible for study design, data collection, data analysis, draft report writing and critical revisions. AAN was responsible for data collection and critical revisions. KD was responsible for study design, data analysis support and critical revisions. All authors critically reviewed the manuscript and approved the final version submitted for publication.

References

1. Andréasson A, Arborelius L, Erlanson-Albertsson C *et al.* (2007) A putative role for cytokines in the impaired appetite in depression. *Brain Behav Immun* **21**, 147–152.
2. American Psychiatric Association (2013) *Diagnostic and Statistical Manual of Mental Disorders (DSM-5)*. Washington, DC: American Psychiatric Publication.
3. Norris V, Molina F & Gewirtz AT (2013) Hypothesis: bacteria control host appetites. *J Bacteriol* **195**, 411–416.
4. Foster JA & Neufeld K-AM (2013) Gut–brain axis: how the microbiome influences anxiety and depression. *Trends Neurosci* **36**, 305–312.
5. O'Mahony S, Clarke G, Borre Y *et al.* (2015) Serotonin, tryptophan metabolism and the brain-gut-microbiome axis. *Behav Brain Res* **277**, 32–48.
6. Hakansson A & Molin G (2011) Gut microbiota and inflammation. *Nutrients* **3**, 637–682.
7. Maes M, Berk M, Goehler L *et al.* (2012) Depression and sickness behavior are Janus-faced responses to shared inflammatory pathways. *BMC Med* **10**, 66.
8. Maes M, Yirmyia R, Noraberg J *et al.* (2009) The inflammatory & neurodegenerative (I&ND) hypothesis of depression: leads for future research and new drug developments in depression. *Metab Brain Dis* **24**, 27–53.
9. Heisler LK, Pronchuk N, Nonogaki K *et al.* (2007) Serotonin activates the hypothalamic–pituitary–adrenal axis via serotonin 2C receptor stimulation. *J Neurosci* **27**, 6956–6964.
10. Du X & Pang TY (2015) Is dysregulation of the HPA-axis a core pathophysiology mediating co-morbid depression in neurodegenerative diseases? *Front Psychiatry* **6**, 32.
11. Kovatcheva-Datchary P & Arora T (2013) Nutrition, the gut microbiome and the metabolic syndrome. *Best Pract Res Clin Gastroenterol* **27**, 59–72.
12. Hill C, Guarner F, Reid G *et al.* (2014) Expert consensus document: the International Scientific Association for Probiotics and Prebiotics consensus statement on the scope and appropriate use of the term probiotic. *Nat Rev Gastroenterol Hepatol* **11**, 506–514.
13. Schrezenmeir J & de Vrese M (2001) Probiotics, prebiotics, and synbiotics – approaching a definition. *Am J Clin Nutr* **73**, 361s–364s.
14. Million M, Angelakis E, Paul M *et al.* (2012) Comparative meta-analysis of the effect of Lactobacillus species on weight gain in humans and animals. *Microb Pathog* **53**, 100–108.
15. Sanchez M, Darimont C, Panahi S *et al.* (2017) Effects of a diet-based weight-reducing program with probiotic supplementation on satiety efficiency, eating behaviour traits, and psychosocial behaviours in obese individuals. *Nutrients* **9**, E284.
16. Liber A & Szajewska H (2013) Effects of inulin-type fructans on appetite, energy intake, and body weight in children and adults: systematic review of randomized controlled trials. *Ann Nutr Metab* **63**, 42–54.
17. Steenbergen L, Sellaro R, van Hemert S, Bosch JA & Colzato LS (2015) A randomized controlled trial to test the effect of multispecies probiotics on cognitive reactivity to sad mood. *Brain Behav Immun.* **48**, 258–264.
18. Akkasheh G, Kashani-Poor Z, Tajabadi-Ebrahimi M *et al.* (2016) Clinical and metabolic response to probiotic administration in patients with major depressive disorder: a randomized, double-blind, placebo-controlled trial. *Nutrition* **32**, 315–320.
19. Messaoudi M, Violle N, Bisson J-F *et al.* (2011) Beneficial psychological effects of a probiotic formulation (*Lactobacillus helveticus* R0052 and *Bifidobacterium longum* R0175) in healthy human volunteers. *Gut Microbes* **2**, 256–261.
20. Kazemi A, Noorbala AA, Azam K *et al.* (2018) Effect of probiotic and prebiotic vs placebo on psychological outcomes in patients with major depressive disorder: a randomized clinical trial. *Clin Nutr* **38**, 522–528.
21. Parker BA, Sturm K, MacIntosh C *et al.* (2004) Relation between food intake and visual analogue scale ratings of appetite and other sensations in healthy older and young subjects. *Eur J Clin Nutr* **58**, 212.
22. Tahavorgar A, Vafa M, Shidfar F *et al.* (2014) Whey protein preloads are more beneficial than soy protein preloads in regulating appetite, calorie intake, anthropometry, and body composition of overweight and obese men. *Nutr Res* **34**, 856–861.
23. Lindeman A, Huang M & Dawkins E (2016) Using the visual analog scale (VAS) to measure perceived hunger and satiety at various mealtimes and environments. *J Acad Nutr Diet* **116**, A99.
24. Kazemi A, Noorbala AA, Azam K, Eskandari MH & Djafarian K (2019) Effect of probiotic and prebiotic vs placebo on psychological outcomes in patients with major depressive disorder: A randomized clinical trial. *Clin Nutr.* **38**(2), 522–528.
25. Diop L, Guillou S & Durand H (2008) Probiotic food supplement reduces stress-induced gastrointestinal symptoms in volunteers: a double-blind, placebo-controlled, randomized trial. *Nutr Res* **28**, 1–5.
26. Wang H, Lee I-S, Braun C *et al.* (2016) Effect of probiotics on central nervous system functions in animals

and humans: a systematic review. *J Neurogastroenterol Motil* **22**, 589.
27. Felger JC & Lotrich FE (2013) Inflammatory cytokines in depression: neurobiological mechanisms and therapeutic implications. *Neuroscience* **246**, 199–229.
28. Schmidt K, Cowen PJ, Harmer CJ *et al.* (2014) Prebiotic intake reduces the waking cortisol response and alters emotional bias in healthy volunteers. *Psychopharmacology* **232**, 1793–1801.
29. Silk D, Davis A, Vulevic J *et al.* (2009) Clinical trial: the effects of a trans-galactooligosaccharide prebiotic on faecal microbiota and symptoms in irritable bowel syndrome. *Aliment Pharmacol Ther* **29**, 508–518.
30. Plata-Salamán CR (2000) Central nervous system mechanisms contributing to the cachexia–anorexia syndrome. *Nutrition* **16**, 1009–1012.
31. Dantzer R (2001) Cytokine-induced sickness behavior: mechanisms and implications. *Ann NY Acad Sci* **933**, 222–234.
32. Wong S & Pinkney J (2004) Role of cytokines in regulating feeding behaviour. *Curr Drug Targets* **5**, 251–263.
33. Eisenberger NI, Berkman ET, Inagaki TK *et al.* (2010) Inflammation-induced anhedonia: endotoxin reduces ventral striatum responses to reward. *Biol Psychiatry* **68**, 748–754.
34. Brydon L, Harrison NA, Walker C *et al.* (2008) Peripheral inflammation is associated with altered substantia nigra activity and psychomotor slowing in humans. *Biol Psychiatry* **63**, 1022–1029.
35. Höflich A, Michenthaler P, Kasper S *et al.* (2018) Circuit mechanisms of reward, anhedonia, and depression. *Int J Neuropsychopharmacol* **22**, 105–118.
36. Lanzenberger R, Kranz GS, Haeusler D *et al.* (2012) Prediction of SSRI treatment response in major depression based on serotonin transporter interplay between median raphe nucleus and projection areas. *NeuroImage* **63**, 874–881.
37. Hahn A, Haeusler D, Kraus C *et al.* (2014) Attenuated serotonin transporter association between dorsal raphe and ventral striatum in major depression. *Hum Brain Mapp* **35**, 3857–3866.
38. Kraus C, Ganger S, Losak J *et al.* (2014) Gray matter and intrinsic network changes in the posterior cingulate cortex after selective serotonin reuptake inhibitor intake. *NeuroImage* **84**, 236–244.
39. Cani PD, Lecourt E, Dewulf EM *et al.* (2009) Gut microbiota fermentation of prebiotics increases satietogenic and incretin gut peptide production with consequences for appetite sensation and glucose response after a meal. *Am J Clin Nutr* **90**, 1236–1243.
40. Harrold J, Hughes G, O'Shiel K *et al.* (2013) Acute effects of a herb extract formulation and inulin fibre on appetite, energy intake and food choice. *Appetite* **62**, 84–90.
41. Hess JR, Birkett AM, Thomas W *et al.* (2011) Effects of short-chain fructooligosaccharides on satiety responses in healthy men and women. *Appetite* **56**, 128–134.
42. Karalus M, Clark M, Greaves KA *et al.* (2012) Fermentable fibers do not affect satiety or food intake by women who do not practice restrained eating. *J Acad Nutr Diet* **112**, 1356–1362.
43. Verhoef SP, Meyer D & Westerterp KR (2011) Effects of oligofructose on appetite profile, glucagon-like peptide 1 and peptide YY3-36 concentrations and energy intake. *Br J Nutr* **106**, 1757–1762.
44. Reimer RA, Willis HJ, Tunnicliffe JM *et al.* (2017) Inulin-type fructans and whey protein both modulate appetite but only fructans alter gut microbiota in adults with overweight/obesity: a randomized controlled trial. *Mol Nutr Food Res* **61**, . Epub 2017 Aug 29 https://doi.org/10.1002/mnfr.201700484.
45. Hume MP, Nicolucci AC & Reimer RA (2017) Prebiotic supplementation improves appetite control in children with overweight and obesity: a randomized controlled trial. *Am J Clin Nutr* **105**, 790–799.
46. Naruszewicz M, Johansson ML, Zapolska-Downar D *et al.* (2002) Effect of Lactobacillus plantarum 299v on cardiovascular disease risk factors in smokers. *Am J Clin Nutr* **76**, 1249–1255.
47. Sherf-Dagan S, Zelber-Sagi S, Zilberman-Schapira G *et al.* (2018) Probiotics administration following sleeve gastrectomy surgery: a randomized double-blind trial. *Int J Obes* **42**, 147–155.
48. Zarrati M, Salehi E, Nourijelyani K *et al.* (2014) Effects of probiotic yogurt on fat distribution and gene expression of proinflammatory factors in peripheral blood mononuclear cells in overweight and obese people with or without weight-loss diet. *J Am Coll Nutr* **33**, 417–425.
49. Sanchez M, Darimont C, Drapeau V *et al.* (2014) Effect of Lactobacillus rhamnosus CGMCC1.3724 supplementation on weight loss and maintenance in obese men and women. *Br J Nutr* **111**, 1507–1519.
50. Esel E, Ozsoy S, Tutus A *et al.* (2005) Effects of antidepressant treatment and of gender on serum leptin levels in patients with major depression. *Prog Neuropsychopharmacol Biol Psychiatry* **29**, 565–570.
51. Pariante CM & Miller AH (2001) Glucocorticoid receptors in major depression: relevance to pathophysiology and treatment. *Biol Psychiat* **49**, 391–404.
52. Hatzinger M (2000) Neuropeptides and the hypothalamic-pituitary-adrenocortical (HPA) system: review of recent research strategies in depression. *World J Biol Psychiatry* **1**, 105–111.
53. Luo J, Rizkalla SW, Alamowitch C *et al.* (1996) Chronic consumption of short-chain fructooligosaccharides by healthy subjects decreased basal hepatic glucose production but had no effect on insulin-stimulated glucose metabolism. *Am J Clin Nutr* **63**, 939–945.

54. Giacco R, Clemente G, Luongo D *et al.* (2004) Effects of short-chain fructo-oligosaccharides on glucose and lipid metabolism in mild hypercholesterolaemic individuals. *Clin Nutr* **23**, 331–340.
55. Jackson KG, Taylor GR, Clohessy AM *et al.* (1999) The effect of the daily intake of inulin on fasting lipid, insulin and glucose concentrations in middle-aged men and women. *Br J Nutr* **82**, 23–30.
56. Parnell JA & Reimer RA (2009) Weight loss during oligofructose supplementation is associated with decreased ghrelin and increased peptide YY in overweight and obese adults. *Am J Clin Nutr* **89**, 1751–1759.
57. Genta S, Cabrera W, Habib N *et al.* (2009) Yacon syrup: beneficial effects on obesity and insulin resistance in humans. *Clin Nutr* **28**, 182–187.

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NUTRITIONAL EPIDEMIOLOGY

Association between soft drink, fruit juice consumption and obesity in Eastern Europe: cross-sectional and longitudinal analysis of the HAPIEE study

A. Garduño-Alanís[1,2] S. Malyutina,[3,4] A. Pajak,[5] U. Stepaniak,[5] R. Kubinova,[6] D. Denisova,[3] H. Pikhart,[1] A. Peasey,[1] M. Bobak[1] & D. Stefler[1]

[1]Department of Epidemiology and Public Health, University College London, London, UK
[2]Research Department, Universidad de la Salud del Estado de México, Toluca, México
[3]Research Institute of Internal and Preventive Medicine – Branch of the Institute of Cytology and Genetics, Siberian Branch of Russian Academy of Sciences, Novosibirsk, Russia
[4]Novosibirsk State Medical University, Novosibirsk, Russia
[5]Department of Epidemiology and Population Studies, Jagiellonian University Collegium Medicum, Krakow, Poland
[6]National Institute of Public Health, Prague, Czech Republic

Keywords
body mass index, Eastern Europe, fruit juice, soft drinks.

Correspondence
A. Garduño-Alanís, Research Department, Universidad de la Salud del Estado de México, Vialidad Toluca Atlacomulco 1946 Col. La Aviación, C.P.50295, Toluca, Edomex, México.
Tel.: +52 722 3917120
E-mail: a.garduno-alanis.17@ucl.ac.uk

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Abstract

Background: Fruit juice and soft drink consumption have been shown to be related to obesity. However, this relationship has not been explored in Eastern Europe. The present study aimed to assess the cross-sectional and longitudinal relationships between fruit juice, soft drink consumption and body mass index (BMI) in Eastern European cohorts.
Methods: Data from the Health, Alcohol and Psychosocial factors in Eastern Europe population-based prospective cohort study, based in Russia, Poland and the Czech Republic, were used. Intakes of sugar-sweetened beverage (SSB), artificially-sweetened beverage (ASB) and fruit juice were estimated from a food frequency questionnaire. Participant BMI values were assessed at baseline (n = 26 634) and after a 3-year follow-up (data available only for Russia, n = 5205).
Results: Soft drink consumption was generally low, particularly in Russia. Compared to never drinkers of SSB, participants who drank SSB every day had a significantly higher BMI in the Czech [β-coefficient = 0.28; 95% confidence interval (CI) = 0.02–0.54], Russian (β-coefficient = 1.38; 95% CI = 0.62–2.15) and Polish (β-coefficient = 0.83; 95% CI = 0.29–1.37) cohorts. Occasional or daily ASB consumption was also positively associated with BMI in all three cohorts. Results for daily fruit juice intake were inconsistent, with a positive association amongst Russians (β-coefficient = 0.75; 95% CI = 0.28–1.21) but a negative trend in the Czech Republic (β-coefficient = −0.42; 95% CI = −0.86 to 0.02). Russians participants who drank SSB or ASB had an increased BMI after follow-up.
Conclusions: Our findings support previous studies suggesting that soft drink consumption (including SSBs and ASBs) is positively related to BMI, whereas our results for fruit juice were less consistent. Policies regarding these beverages should be considered in Eastern Europe to lower the risk of obesity.

Introduction

Cardiovascular disease (CVD) mortality and morbidity rates in Eastern European countries (EECs) are considerably higher than in the West [1]. This health gap emerged in the 1970s, became more pronounced after the political reconstruction in the early 1990s and, despite some reduction in recent years, it still exists today [2].

It is likely that unhealthy diet has contributed to the high CVD rates in EECs [2–4]. For example, the subsidy of foods with a high saturated fat content could have contributed to the excessive consumption of such products before the 1990s [3]. More recent data from EEC show that intakes of saturated fats, sugar and meat products are still too high, whereas the consumption of fruits and vegetables is lower than World Health Organization (WHO) recommendations [5,6]. Other diet-related risk factors, such as obesity, could have also contributed to the health gap between Eastern and Western Europe. Obesity rates have almost tripled over the last 30 years globally [7,8], and similar trends can be observed in EEC. [9,10] Projections suggest a considerable further increase in the prevalence of obesity in EECs by 2050 [11].

The consumption of soft drinks, including sugar-sweetened beverages (SSBs) and artificial-sweetened beverages (ASB), has increased substantially during the past decades in most parts of the world [12]. Although Eastern Europeans are considered to be low consumers in this aspect [13], increasing trends can be observed here too, particularly after the political reconstruction in 1990 [12]. Because most previous studies show that regular soft drink consumption is related to a higher body mass index (BMI), these products may be partly responsible for the global obesity epidemic [14–17]. However, the available evidence is not entirely consistent [18,19]. A similar debate has emerged regarding fruit juice consumption [20,21]. Although moderate fruit juice intake may provide nutritional benefits and does not appear to have a negative impact on body weight measures, [20] some studies have shown that their regular intake was positively associated with long-term weight gain [21].

Consumption patterns of soft drinks and fruit juices have not been explored in Eastern European adults, and their association with obesity within this region has not been assessed. Using data from the Health, Alcohol and Psychosocial Factors in Eastern Europe (HAPIEE) prospective cohort study, we examined the cross-sectional relationship between fruit juice/soft drink consumption and obesity in Russian, Czech and Polish cohorts, and we explored whether these drinks affect BMI change over time in the Russian cohort where follow-up data were available.

Materials and methods

Study sample

The HAPIEE study is a multicentre prospective cohort study with participants recruited in Russia, Poland and Czech Republic [22]. The cohorts in each country consisted of random samples of men and women aged 45–69 years at baseline, who were selected from population registers in Novosibirsk (Russia), Krakow (Poland) and six towns in the Czech Republic, stratified by gender and 5-year age groups. The overall response rate was 59% [22].

From 28 945 participants at baseline, those who had missing data on the exposure ($n = 718$), outcome ($n = 46$) and covariates ($n = 1283$) were excluded from the sample. Individuals with extreme values for weight (more than 200 kg), height (more than 205 cm) and energy intake (more than 5000 kcal day^{-1} or less than 500 kcal day^{-1}) were also excluded ($n = 264$). After these exclusions, the analytical sample for the cross-sectional assessment consisted of 26 634 individuals. In addition to the cross-sectional analysis with baseline measurements, BMI change over time was assessed in the Russian cohort. From the 6182 individuals who participated in the second wave of the study in this country, data on height and weight measurements were available for 5205 people.

Data collection

Baseline survey (wave 1) was conducted between 2002 and 2005. In Russia, questionnaires and examinations were carried out in a clinic. In Poland and the Czech Republic, questionnaires were completed at home and examinations were carried out in a clinic. The structured questionnaires covered health, lifestyle, food frequency, socioeconomic circumstances, psychosocial factors and psychosocial environment at work. The examination included anthropometric, physical, cognitive and blood evaluations. The cohorts were re-interviewed in 2006–2008 (wave 2) [22], although height and weight were measured only in Russian participants; therefore, longitudinal evaluations analyses could not be performed in the Polish and Czech cohorts.

Participants were asked 'how often, on average in the last 3 months they consumed specific foods and drinks', details of this dietary data collection procedures with food frequency questionnaires (FFQ) have been described earlier [23]. The FFQ item that asked the participants about the intake of non-alcoholic carbonated (fizzy) drinks, such as coke, fizzy orange or lemonade, was used to estimate SSB consumption, whereas the item on low-calorie (diet) carbonated drinks was used for ASB. Fruit juice intake was also assessed with one FFQ item which

asked about the intake of fruit juices, such as apple drinks. For all fruit juice and soft drinks, one drink was equivalent to 200 mL. For the current analysis, all participants were classified into three categories of their SSB, ASB or fruit juice consumption: never drinkers, occasional drinkers (less than one drink per day) and daily drinkers (one or more drinks per day). Three categories were specified to assess the gradient in the potential effect and not just the difference between drinkers and non-drinkers.

Measured and self-reported height and weight were used to calculate the BMI. Height was measured using a mechanical stadiometer and weight was assessed with an electronic scale (both measurements were obtained without shoes and outer clothes) [23]. At baseline, 3085 (10.7%) participants had missing data on either measured weight or measured height; to avoid losing so many subjects, missing data of measured weight and height were replaced by self-reported weight and height, respectively. This replacement was based on a high correlation between the measured and self-reported data in participants with both indicators available ($r = 0.97$, $r = 0.95$). For further confirmation, we also ran the analysis on participants with measured BMI values, and the results obtained were similar to our main findings. BMI was calculated dividing body weight by the square of body height (kg m^{-2}). In line with the WHO categorisation of BMI for adult population, obesity was defined as BMI $\geq$30 kg m^{-2}.

In the second wave of data collection in the Russian cohort, measured height and weight was used to calculate BMI. The change in BMI was obtained by subtracting BMI at baseline from BMI in wave 2.

Ethical approval

All participants provided informed consent prior to their inclusion in the study. Study protocols were approved by ethical committees at University College London, and all participating centres in Poland, Russia and the Czech Republic and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Statistical analysis

The cross-sectional associations between the exposure (fruit juice, SSB and ASB consumption) and outcome (BMI) variables were assessed with multivariable-adjusted linear and logistic regression models. In the linear regression, BMI was used as continuous variable, whereas, in the logistic regression models, BMI was dichotomised in two categories: obese (BMI $\geq$30 kg m^{-2}) and non-obese (BMI <30 kg m^{-2}). All associations were assessed in three models. In model 1, these were adjusted for age and sex. In model 2, they were further adjusted for socio-demographic variables, such as education and marital status. Finally, in model 3, lifestyle factors that can act as potential confounders, including smoking, alcohol consumption, physical activity, energy intake and fruit and vegetable consumption, as well as previously diagnosed chronic diseases, such as diabetes, CVD or cancer, were also included.

Because we found statistically significant heterogeneity in country cohort-specific associations of SSB, ASB and fruit juice consumption with BMI ($P < 0.001$), all results are presented separately in the Czech, Polish and Russian samples, and pooled results are not shown. No other covariates emerged as significant effect modifiers across the three cohorts.

In the longitudinal analysis, associations between the exposure (fruit juice, SSB and ASB) and changes in BMI were examined using multivariable logistic regression models. For this analysis, an increase in BMI of more than 1 kg m^{-2} between wave 1 and 2 was used as the main outcome variable. As a result of the low number of daily soft drink consumers and the consequent impact on statistical power, in this part of the analysis, we compared only two categories of participants: drinkers and non-drinkers.

All tests were performed with STATA, version 15 (StataCorp, College Station, TX, USA). $P < 0.05$ was considered statistically significant.

Results

Descriptive characteristics of the sample are shown in Table 1. The mean BMI in the analytical sample was 28 kg m^{-2} or higher in all three cohorts. With the exception of SSB intake among Czech participants, soft drink consumption was generally low, particularly in Russia, where the prevalence of daily SSB and ASB consumption was <2% and 1%, respectively. Fruit juice consumption was also found to be relatively low, with less than 10% of the sample reported to drink it every day in Russia and the Czech Republic.

In the bivariate analysis (Table 2), almost all of the covariates were associated with fruit juice, SSB and ASB consumption in the pooled sample. Daily fruit juice consumption was found to be considerably more common in females, participants with higher education and abstainers from alcohol, as well as among those who reported higher physical activity. By contrast, regular SSB intake was more common in males, individuals with lower education and regular alcohol drinkers, as well as in those who reported less exercise. Both SSB and ASB were more common in

Table 1 Descriptive characteristics of the study sample by country (n = 26 634)

Variable	Country			
	Czech (n = 7741)	Russia (n = 9218)	Poland (n = 9675)	Total (n = 26 634)
BMI (kg m^{-2}), mean (SD)	28.1 (4.5)	28.5 (5.5)	28.0 (4.6)	28.2 (5)
Fruit juice consumption, *n* (%)				
Never drink	3503 (45.2)	3672 (39.8)	2477 (25.6)	9652 (36.2)
<1 per day	3796 (49.0)	4992 (54.2)	5456 (56.4)	14 244 (53.5)
≥1 per day	442 (5.7)	554 (6.0)	1742 (18.0)	2738 (10.3)
Soft drinks				
SSB consumption, *n* (%)				
Never drink	3621 (46.8)	7142 (77.5)	7935 (82.0)	18 698 (70.2)
<1 per day	2386 (30.8)	1903 (20.6)	1468 (15.2)	5757 (21.6)
≥1 per day	1734 (22.4)	173 (1.9)	272 (2.8)	2179 (8.2)
ASB consumption, *n* (%)				
Never drink	5697 (73.6)	8961 (97.2)	8156 (84.3)	22 814 (85.7)
<1 per day	1480 (19.1)	205 (2.2)	908 (9.4)	2593 (9.7)
≥1 per day	564 (7.3)	52 (0.6)	611 (6.3)	1227 (4.6)
Age group (years), *n* (%)				
<55	2913 (37.6)	3341 (36.2)	3793 (39.2)	10 047 (37.7)
55–65	3212 (41.5)	3724 (40.4)	3950 (40.8)	10 886 (40.9)
>65	1616 (20.9)	2153 (23.4)	1932 (20.0)	57.01 (21.4)
Sex, *n* (%)				
Men	3642 (47.0)	4164 (45.2)	4703 (48.6)	12 509 (47.0)
Woman	4099 (53.0)	5054 (54.8)	4972 (51.4)	14 125 (53.0)
Education, *n* (%)				
Primary or less	900 (11.6)	967 (10.5)	1124 (11.6)	2991 (11.2)
Vocational	2802 (36.2)	2445 (26.5)	2034 (21.0)	7281 (27.3)
Secondary	2912 (37.6)	3146 (34.1)	3748 (38.7)	9806 (36.8)
University degree	1127 (14.6)	2660 (28.9)	2769 (28.6)	6556 (24.6)
Marital status, *n* (%)				
Living with a partner	5903 (76.3)	6649 (72.1)	7384 (76.3)	19 936 (74.8)
Living without a partner	1838 (23.7)	2569 (27.9)	2291 (23.7)	6698 (25.2)
Smoking, *n* (%)				
Never smoker	3370 (43.5)	5377 (58.3)	3832 (39.6)	12 579 (47.2)
Ex-smoker	2315 (30.0)	1255 (13.6)	2733 (28.3)	6303 (23.7)
Regular smoker	2056 (26.6)	2586 (28.1)	3110 (32.1)	7752 (29.1)
Alcohol consumption (g day^{-1}), *n* (%)				
0	921 (11.9)	1472 (16.0)	3289 (34.0)	5682 (21.3)
>0–20	5494 (71.0)	6630 (72.0)	5797 (60.0)	17 921 (67.3)
>20	1326 (17.1)	1116 (12.1)	589 (6.1)	3031 (11.4)
Physical activity (MET-h day^{-1}), *n* (%)				
<5	2711 (35.0)	2638 (28.6)	2861 (29.6)	8210 (30.8)
5–15	3809 (49.2)	5245 (56.9)	5083 (52.5)	14 137 (53.1)
>15	1221 (15.8)	1335 (14.5)	1731 (17.9)	4287 (16.1)
Energy (kcal day^{-1}), *n* (%)				
<2000	4320 (55.8)	2419 (26.2)	4351 (45.0)	11 090 (41.7)
2000–2500	1884 (24.3)	2487 (27.0)	2857 (29.5)	7228 (27.1)
>2500	1537 (19.9)	4312 (46.8)	2467 (25.5)	8316 (31.2)
Fruits and vegetables consumption (g day^{-1}), *n* (%)				
<300	1825 (23.6)	3531 (38.3)	2500 (25.8)	7856 (29.5)
300–600	3064 (39.6)	4154 (45.1)	4485 (46.4)	11 703 (44.0)
>600	2852 (36.8)	1533 (16.6)	2690 (27.8)	7075 (26.6)
CVD or cancer in medical history, *n* (%)				
No	6664 (86.1)	7808 (84.7)	8196 (84.7)	22 668 (85.1)
Yes	1077 (13.9)	1410 (15.3)	1479 (15.3)	3966 (14.9)

Table 1 Continued

Variable	Country			
	Czech (n = 7741)	Russia (n = 9218)	Poland (n = 9675)	Total (n = 26 634)
Diabetes in medical history, n (%)				
No	6863 (88.7)	8728 (95.7)	8571 (88.6)	24 162 (90.7)
Yes	878 (11.3)	490 (5.3)	1104 (11.4)	2472 (9.3)

ASB, artificially sweetened beverages; BMI, body mass index; CVD, cardiovascular disease; MET, metabolic equivalents; SSB, sugar-sweetened beverages.

younger compared to older participants, as well as among regular smokers and among those who eat high amounts of fruits and vegetables. These results were largely similar if the associations were examined separately in the three countries (data not shown).

Table 3 shows the results of the multivariable-adjusted linear regression analysis for the association of fruit juice, SSB and ASB consumption with BMI, separately by country-cohorts.

Participants who drank fruit juice every day had significantly higher BMI compared to never drinkers in the Russian sample, and a similar positive trend, although statistically not significant, was found in Poland. However, the direction of the association was the opposite in the Czech cohort, indicating lower BMI among daily fruit juice drinkers with borderline statistical significance after multivariable adjustment.

Regarding SSB, we found a positive association with a clear dose–response gradient across occasional and daily drinkers in all three cohorts. Compared to never drinkers, individuals with occasional or regular ASB intake had a significantly higher BMI in the Czech and Polish cohorts, whereas this positive association was statistically significant among occasional drinkers in Russia.

Results were similar when the associations were examined with logistic regression models using obesity (BMI > 30 kg m^{-2}), as the main outcome variable (n = 8358) (see Supporting information, Table S1).

Table 4 shows the results of the multivariable logistic regression models for the association between fruit juice/soft drink consumption and an increase in BMI of more than 1 kg m^{-2} over an average follow-up of 3 years among Russian participants. BMI increased by more than 1 kg m^{-2} in 1789 participants (34.4% of the sample), whereas it decreased or increased <1 kg m^{-2} in 3416 people (65.6%). The mean (SD) change of BMI in these groups was 2.4 (2.6) kg m^{-2} and −0.56 (1.3) kg m^{-2}, respectively. We found that SSB and ASB intake was significantly related to BMI increase. On the other hand, fruit juice consumption was associated with lower risk of BMI increase but this association was not statistically significant.

Discussion

Main findings

In the present study investigating soft drink and fruit juice consumption in three Eastern European cohorts, we found a relatively low prevalence of daily consumption of both, particularly in Russia. Despite some inconsistencies across cohorts, the cross-sectional analyses indicated that occasional or daily SSB and ASB consumptions were related to higher BMI. The prospective analysis of the Russian cohort also suggested that individuals who occasionally drank these food products had a higher risk of increased BMI at follow-up. The results on fruit juice consumption were inconsistent because the BMI of regular drinkers, compared to never drinkers, appeared to be higher in the Russia and Poland but lower in the Czech Republic.

Interpretation of the results

Overall, 10.3% of the participants reported that they drank fruit juice every day, which is lower than the intakes reported for Western European countries. [16] The observed rates of daily soft drink consumption of 8.2% and 4.6% for SSB and ASB, respectively, are low compared to global reports from 2016 [13,16] . However, the mean age of our respondents was 58 years, and drinking of SSB is much more common at a younger age. For example, everyday consumption of fruit juice was observed in 28% and SBB in 17% of young people in Poland. [24] Furthermore, because the data for the present study were collected in 2002–2004, consumption habits may have subsequently changed. Nevertheless, more recent surveys also suggest a relatively low intake of sugary drinks in Russia [25].

Our results for the association between soft drinks, fruit juice consumption and BMI are generally consistent with existing literature. Previously published studies that examined the link between fruit juice intake and obesity often produced conflicting results [26,27]. Although fruit juice consumption has been associated with a small amount of long-term weight gain [28], a moderate amount

Table 2 Bivariate analysis of main exposure and covariates

		Fruit juice consumption				SSB consumption				ASB consumption			
	Total n = 26 634 (%)	Never drink, n = 9652 (%)	<1 per day, n = 14 244 (%)	≥1 per day, n = 2738 (%)	P value† (P for trend‡)	Never drink, n = 18698 (%)	<1 per day, n = 5757 (%)	≥1 per day, n = 2179 (%)	P value† (P for trend‡)	Never drink, n = 228 14 (%)	<1 per day, n = 2593 (%)	≥1 per day, n = 1227 (%)	P value† (P for trend‡)
Covariates													
Socio-demographics													
Age (years)*													
<55	10 047 (100)	27.4	59.8	12.8	<0.001 (<0.001)	63.2	26.9	9.9	<0.001 (<0.001)	83.3	11.7	5.0	<0.001 (0.004)
55–65	10 886 (100)	38.2	52.0	9.8		72.5	19.9	7.6		86.3	9.1	4.6	
>65	5701 (100)	48.1	45.1	6.8		78.1	15.6	6.3		88.5	7.5	4.0	
Sex													
Men	12 509 (100)	38.0	53.4	8.6	<0.001	63.9	26.2	9.9	<0.001	84.2	11.0	4.7	<0.001
Women	14 125 (100)	34.7	53.6	11.7		75.7	17.6	6.7		87.0	8.6	4.5	
Education*													
Primary or less	2991 (100)	51.7	42.2	6.1	<0.001 (<0.001)	70.9	19.9	9.2	<0.001 (<0.001)	85.0	10.0	5.0	<0.001 (<0.001)
Vocational	7281 (100)	40.4	51.5	8.1		65.0	22.5	12.5		83.4	11.2	5.4	
Secondary	9806 (100)	35.3	54.7	10.0		70.2	22.7	7.1		85.9	9.5	4.6	
University degree	6556 (100)	26.0	59.1	14.9		75.6	19.9	4.5		88.1	8.3	3.6	
Marital status													
Living with a partner	19 936 (100)	35.0	54.5	10.5	<0.001	68.7	22.7	8.7	<0.001	84.9	10.3	4.8	<0.001
Living alone	6698 (100)	39.9	50.5	9.6		74.8	18.5	6.7		88.0	8.2	3.8	
Lifestyle behaviours/medical history													
Smoking													
Never smoker	12 579 (100)	34.9	55.3	9.8	<0.001	73.3	20.2	6.5	<0.001	87.7	8.5	3.8	<0.001
Ex-smoker	6303 (100)	37.5	51.8	10.7		69.5	21.2	9.3		82.7	11.4	5.9	
Regular smoker	7752 (100)	37.4	51.8	10.8		65.7	24.2	10.1		84.8	10.3	4.9	
Alcohol consumption (g day^{-1})*													
0	5682 (100)	39.7	48.7	11.6	<0.001 (<0.001)	81.2	13.9	4.9	<0.001 (<0.001)	86.5	7.7	5.8	<0.001 (<0.001)
>0–20	17 921 (100)	34.2	55.5	10.3		69.0	22.6	8.4		85.7	10.0	4.3	
>20	3031 (100)	42.0	50.5	7.5		56.7	30.5	12.8		84.1	11.6	4.3	
Physical activity (MET-h day^{-1})*													
<5	8210 (100)	38.9	51.2	9.9	<0.001 (<0.01)	67.5	22.4	10.1	<0.001 (<0.01)	85.6	10.2	4.2	<0.001 (<0.001)
5–15	14 137 (100)	34.5	55.4	10.1		70.6	21.9	7.5		85.9	9.7	4.4	
>15	4287 (100)	36.9	51.5	11.6		74.2	19.2	6.6		84.9	8.8	6.3	
Energy (kcal day^{-1})*													
<2000	11 090 (100)	43.3	50.3	6.5	<0.001 (<0.001)	74.0	18.9	7.1	<0.001 (<0.001)	85.1	10.1	4.8	0.222 (0.530)

Table 2 Continued

		Fruit juice consumption				SSB consumption				ASB consumption			
	Total n = 26 634 (%)	Never drink, n = 9652 (%)	<1 per day, n = 14 244 (%)	≥1 per day, n = 2738 (%)	P value[†] (P for trend[‡])	Never drink, n = 18698 (%)	<1 per day, n = 5757 (%)	≥1 per day, n = 2179 (%)	P value[†] (P for trend[‡])	Never drink, n = 228 14 (%)	<1 per day, n = 2593 (%)	≥1 per day, n = 1227 (%)	P value[†] (P for trend[‡])
2000–2500	7228 (100)	34.6	54.9	11.0		70.6	21.5	7.9		85.2	9.9	4.4	
>2500	8316 (100)	28.3	56.9	14.8		64.8	25.3	9.9		86.2	9.2	4.6	
Fruits and vegetables consumption (g day^{-1})*													
<300	7856 (100)	47.3	47.7	5.0	<0.001 (<0.001)	69.4	23.2	7.4	<0.001 (<0.001)	89.5	7.6	2.9	<0.001 (<0.001)
300–600	11 703 (100)	33.0	57.2	9.8		71.4	21.0	7.6		85.9	9.5	4.6	
>600	7075 (100)	29.3	53.7	17.0		69.1	20.8	10.1		81.1	12.5	6.4	
CVD or cancer in medical history													
No	22 668 (100)	35.3	54.4	10.4	<0.001	69.2	22.4	8.4	<0.001	85.7	9.8	4.5	<0.001
Yes	3966 (100)	41.9	48.4	9.7		75.7	17.4	6.9		85.7	9.2	5.1	
Diabetes in medical history													
No	24 162 (100)	34.8	54.7	10.5	<0.001	68.9	22.5	8.6	<0.001	86.5	9.4	4.1	<0.001
Yes	2472 (100)	50.7	41.3	8.0		83.0	13.1	3.9		78.0	12.8	9.2	

ASB, artificially sweetened beverages; CVD cardiovascular disease; MET, metabolic equivalents; SSB, sugar-sweetened beverages.
*To test χ^2 for trend, the main exposure variables were re-categorised in a binary outcome: (never drink + <1 per day) versus (≥1 per day).
†χ^2.
‡χ^2 for trend. $P < 0.05$ was considered statistically significant.

Table 3 Multivariable linear regression for body mass index and fruit juice/soft drink consumption, by country

				Model 1			Model 2			Model 3		
Country	Exposure	Intake level	*n*	β coeff.	95% CI	*P* value	β coeff.	95% CI	*P* value	β coeff.	95% CI	*P* value
Czech	Fruit juice	Never	3505	ref.			ref.			ref.		
		<1 day^{-1}	3796	−0.68	−0.89, −0.47	<0.001	−0.49	−0.70, −0.28	<0.001	−0.30	−0.50, −0.09	0.005
		≥1 day^{-1}	442	−0.83	−1.28, −0.39	<0.001	−0.69	−1.17, −0.24	0.002	−0.42	−0.86, 0.02	0.060
	SSB	Never	3621	ref.			ref.			ref.		
		<1 day^{-1}	2386	−0.16	−0.39, 0.08	0.195	−0.14	−0.37, 0.09	0.233	0.20	−0.02, 0.44	0.081
		≥1 day^{-1}	1734	−0.02	−0.28, 0.24	0.903	−0.21	−0.47, 0.04	0.103	0.28	0.02, 0.54	0.037
	ASB	Never	5697	ref.			ref.			ref.		
		<1 day^{-1}	1480	0.57	0.31, 0.82	<0.001	0.57	0.32, 0.82	<0.001	0.48	0.23, 0.73	<0.001
		≥1 per day	564	1.82	1.43, 2.20	<0.001	1.70	1.32, 2.08	<0.001	1.47	1.09, 1.84	<0.001
Russia	Fruit juice	Never	3672	ref.			ref.			ref.		
		<1 per day	4992	0.14	−0.09, 0.36	0.236	0.18	−0.05, 0.40	0.127	0.13	−0.10, 0.35	0.267
		≥1 per day	554	0.65	0.18, 1.11	0.007	0.77	0.30, 1.25	0.001	0.75	0.28, 1.21	0.002
	SSB	Never	7142	ref.			ref.			ref.		
		<1 per day	1903	0.48	0.15, 0.68	0.002	0.33	0.06, 0.59	0.015	0.49	0.23, 0.75	<0.001
		≥1 per day	173	1.39	0.61, 2.17	<0.001	1.31	0.53, 2.09	0.001	1.38	0.62, 2.15	<0.001
	ASB	Never	8961	ref.			ref.			ref.		
		<1 per day	205	0.99	0.28, 1.71	0.007	0.98	0.27, 1.70	0.007	0.74	0.04, 1.44	0.039
		≥1 per day	52	−0.01	−1.42, 1.40	0.985	−0.02	−1.42, 1.38	0.978	−0.27	−1.64, 1.11	0.704
Poland	Fruit juice	Never	2477	ref.			ref.			ref.		
		<1 per day	5456	−0.05	−0.27, 0.17	0.629	0.12	−0.10, 0.34	0.299	0.20	−0.02, 0.41	0.074
		≥1 per day	1742	−0.06	−0.34, 0.23	0.685	0.21	−0.08, 0.50	0.153	0.25	−0.03, 0.54	0.082
	SSB	Never	7935	ref.	ref.	ref.	ref.	ref.	ref.	ref.	ref.	ref.
		<1 per day	1468	0.21	−0.05, 0.48	0.114	0.21	−0.05, 0.48	0.108	0.41	0.16, 0.67	0.001
		≥1 per day	272	0.58	0.02, 1.14	0.042	0.53	−0.03, 1.08	0.062	0.83	0.29, 1.37	0.003
	ASB	Never	8156	ref.	ref.	ref.	ref.	ref.	ref.	ref.	ref.	ref.
		<1 per day	908	0.26	−0.06, 0.58	0.109	0.21	−0.10, 0.53	0.19	0.30	0.00, 0.61	0.051
		≥1 per day	611	0.80	0.42, 1.18	<0.001	0.80	0.38, 1.14	<0.001	0.62	0.26, 0.99	0.001

ASB, artificially sweetened beverages; CI, confidence interval; coeff., coefficient; ref., reference; SSB, sugar-sweetened beverages.
Model 1: Adjusted for: age + sex. Model 2: model 1 + education + marital status. Model 3: Model 2 + smoking + alcohol consumption + physical activity + energy consumption + fruits and vegetables consumption + cardiovascular disease or cancer in medical history + diabetes in medical history. $P < 0.05$ was considered statistically significant.

Table 4 Multivariable logistic regression for a unit change in body mass index and fruit juice/soft drink consumption, at second wave (2006–2008) in the cohort in Russia (n = 5205)

			Model 1			Model 2			Model 3		
Exposure	Intake level	*n*	OR	95% CI	*P* value	OR	95% CI	*P* value	OR	95% CI	*P* value
Fruit juice	No Drinkers	1963	ref.			ref.			ref.		
	Drinkers	3242	0.90	0.80, 1.02	0.106	0.94	0.83, 1.07	0.368	0.92	0.81, 1.05	0.203
SSB	No Drinkers	4048	ref.			ref.			ref.		
	Drinkers	1157	1.28	1.11, 1.47	<0.001	1.25	1.09, 1.44	0.001	1.26	1.09, 1.45	0.001
ASB	No Drinkers	5091	ref.			ref.			ref.		
	Drinkers	114	1.75	1.21, 2.55	0.003	1.75	1.20, 2.54	0.004	1.63	1.12, 2.39	0.012

ASB, artificially sweetened beverages; CI, confidence interval; coeff., coefficient; ref., reference; SSB, sugar-sweetened beverages.
Body mass index (BMI) change ≥ 1 units (n = 1789; 34.4%) vs. BMI change < 1 units (n = 3416; 65.6%). Model 1: Adjusted for: age + sex. Model 2: model 1 + education + marital status. Model 3: Model 2 + smoking + alcohol consumption + physical activity + energy consumption + fruits and vegetables consumption + BMI at baseline + cardiovascular disease or cancer in medical history + diabetes in medical history. $P < 0.05$ was considered statistically significant. 1 unit change = 1 kg m^{-2}.

of fruit juice could be recommended to different populations without detrimental effects on weight [20]. Because the sugar content of fruit juice is similar or higher than those of whole fruits, whereas it contains much less fibres, its beneficial effect on health is probably weaker compared with fruits [29]. In the present study, the conflicting

results between the Czech and Russian cohorts may be also explained by residual confounding, such as a stronger link between fruit juice intake and a health-conscious lifestyle in the Czech Republic.

Regarding SSB, we found that occasional or everyday consumption was associated with higher BMI in all three cohorts. This result is consistent with previous evidence obtained from other populations, as supported by both observational studies and randomised controlled trials [14,30,31]. For example, in a recent systematic review, among 26 observational studies, only one reported no association between SSB intake and weight gain [30].

In terms of possible mechanism, SSB consumption can lead to weight gain either directly, through higher energy intake from the drinks themselves, or indirectly through energy intake from other food products, because calorie intake from liquid carbohydrates could result in less satiety [32].

Despite the relatively consistent literature, the strength of the relationship between SSB consumption and obesity, as well as the independence of this association from potential confounding factors, is difficult to establish [33]. To overcome the methodological limitations inherent in observational studies and strengthen the evidence further, high-quality randomised controlled trials with adequate design and sample size are clearly warranted [33].

In our analysis, the most consistent positive relationship with obesity was found for ASB intake, also known as diet sodas. As opposed to SSBs, which contain added caloric sweeteners, such as sucrose, high-fructose corn syrup or fruit-juice concentrates, ASBs contain nonsugar sweeteners [34]. Several previous studies on ASB consumption are in accordance with our findings. For example, a higher intake of ASB was found to be related to increased body fat in UK children [35]. Among adults, previous studies found positive relationships of ASB consumption with BMI, abdominal obesity and metabolic syndrome [36–38]. In addition, there is some evidence that increased BMI may play a role in the link between ASB intake and the risk of diabetes [36]. However, the available evidence is inconsistent, and there are several potential explanations for the observed positive associations between ASB intake and obesity. [33] These may include (i) reverse causation, meaning that people tend to drink ASB instead of SSB when they have obesity [38]; (ii) an increase in sweet preference and appetite associated with ASB consumption [39]; and (iii) common artificial sweeteners used in ASB, which could generate a similar body response in terms of satiety compared to SSB [40]. Therefore, future studies that examine the metabolic effects of ASB are still needed.

The results of our longitudinal analysis in Russia are similar to what has been observed in other prospective studies. For example, an increase in body weight of 4–5 kg was found in women whose SSB consumption changed from occasional to everyday over 4 years of follow-up [41]. Another US-based cohort study indicated significant increase in the risk of obesity and overweight over time among those who consumed ASB every day [17,39].

Limitations and strengths

The present study has several limitations that need to be taken into account when interpreting the results.

First, the cross-sectional design of our study does not allow a clear interpretation of temporality, and reverse causation may play a role in some of the observed relationships. For example, people with obesity might reduce their soft drink consumption leading to potential misinterpretation of the main association. Reverse causation might be also the plausible explanation for the observed positive association between ASB intake and obesity. However, the fact that the longitudinal assessment of BMI change over time provided similar results may serve as internal validation and makes this possibility less likely.

Second, the measurement of fruit juice and soft drink intake by FFQ is likely to be imprecise, and this may lead to misclassification of these exposures and inaccurate estimates of the associations. The FFQ is a common method for assessing dietary patterns in epidemiology, although it has been criticised as being imprecise and affected by information bias [42]. Self-reported measures of fruit juice are prone to under- [36] and over-reporting [43], and soft drink consumption is prone to under-reporting [30]. The validity of the dietary data in HAPIEE study was tested using biomarkers regarding fruit and vegetable consumption. However, no such assessment was possible for fruit juice and soft drinks [44]. Similarly, self-reported weight and height were also prone to misclassification of BMI. However, the high completeness of objective measurement and the high correlation between self-reported and measured weight and height make this bias less likely.

Third, the moderate response rates and urban character of the HAPIEE cohorts make is impossible to generalise the findings to the whole population. It is also likely that responders were healthier compared to the general population. However, these issues should not affect the internal validity of our results.

Fourth, although the large sample size is an important strength of the present study, the fact that only a small proportion of participants consumed fruit juice and soft drinks on a regular basis reduces the statistical power of the analysis. This can lead to wide confidence intervals and may be the reason for some of the observed non-significant associations.

Finally, the residual confounding is inherent to the observational study design. Nevertheless, the multiple adjustment for several socio-economic and lifestyle variables reduce this possibility.

The main strengths of the present study are that this is one of the largest cohort studies to investigate the relationship between fruit juice/soft drink consumption and BMI in Eastern Europe. It is also important that the Russian cohort has a longitudinal element allowing assessment of the role of fruit juice/soft drink consumption in BMI change.

Conclusions

Our findings support the hypothesis that soft drink consumption, including both SSBs and ASBs, is positively related to BMI and may lead to obesity. However, the findings regarding the role of fruit juice were inconsistent. Policies regarding soft drink beverages may need to be considered in Eastern Europe to reduce the rates of obesity in the region.

Conflict of interests, source of funding and authorship

The authors declare that they have no conflicts of interest.
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AG-A took part in the concept and design of the analysis, carried out the statistical analysis, interpreted the results and drafted the manuscript. SM, AP and RK contributed to the design of the study, led the field work and critically revised the manuscript. US and DD contributed to the data collection and analysis, and critically revised the manuscript. HP, AP and MB contributed to the conception and design of the HAPIEE study, supported the statistical analyses and critically revised the manuscript. DS contributed to the conception and design of the analysis, supported the statistical analysis, helped to interpret the results and critically revised subsequent drafts of the manuscript. All authors critically reviewed the manuscript and approved the final version submitted for publication.

Transparency declaration

The lead author affirms that this manuscript is an honest, accurate and transparent account of the study being reported. The reporting of this work is compliant with STROBE guidelines. The lead author affirms that no important aspects of the study have been omitted and that any discrepancies from the study as planned have been explained.

References

1. WHO Regional Office for Europe: Health for All Database. Geneva: WHO. Available at: https://gateway.euro.who.int/en/datasets/european-health-for-all-database. (accessed 7 January 2019)
2. Bobak M & Marmot M (1996) East-West mortality divide and its potential explanations: proposed research agenda. *BMJ* **312**, 421–425.
3. Kesteloot H, Sans S & Kromhout D (2006) Dynamics of cardiovascular and all-cause mortality in Western and Eastern Europe between 1970 and 2000. *Eur Heart J* **27**, 107–113.
4. Zatonski WA, McMichael AJ & Powles JW (1998) Ecological study of reasons for sharp decline in mortality from ischaemic heart disease in Poland since 1991. *BMJ* **316**, 1047–1051.
5. Stefler D & Bobak M (2015) Does the consumption of fruits and vegetables differ between Eastern and Western European populations? Systematic review of cross-national studies. *Arch Public Health* **73**, 29.
6. Stefler D, Pajak A, Malyutina S *et al.* (2016) Comparison of food and nutrient intakes between cohorts of the HAPIEE and Whitehall II studies. *Eur J Public Health* **26**, 628–634.
7. World Health Organization (2018) *European Health Information Gateway*. Geneva: WHO. Available at: https://gateway.euro.who.int/ (accessed 19 January 2019).
8. von Ruesten A, Steffen A, Floegel A *et al.* (2011) Trend in Obesity Prevalence in European Adult Cohort Populations during Follow-up since 1996 and Their Predictions to 2015. *PLoS ONE* **6**, 11.
9. Stepaniak U, Micek A, Waśkiewicz A *et al.* (2016) Prevalence of general and abdominal obesity and overweight among adults in Poland. Results of the WOBASZ II study (2013-2014) and comparison with the WOBASZ study (2003-2005). *Pol Arch Med Wewn* **126**, 662–671.
10. Marques A, Peralta M, Naia A *et al.* (2018) Prevalence of adult overweight and obesity in 20 European countries, 2014. *Eur J Public Health* **28**, 295–300.
11. Webber L, Kilpi F, Marsh T *et al.* (2012) Modelling obesity trends and related diseases in Eastern Europe. *Obes Rev* **13**, 744–751.
12. Basu S, McKee M, Galea G *et al.* (2013) Relationship of soft drink consumption to global overweight, obesity, and diabetes: A cross-national analysis of 75 countries. *Am J Pub Health* **11**, 2071–2077.

13. Popkin BM & Hawkes C (2016) Sweetening of the global diet, particularly beverages: patterns, trends, and policy responses. *Lancet Diabet Endocrinol* **4**, 174–186.
14. Malik VS, Pan A, Willett WC *et al.* (2013) Sugar-sweetened beverages and weight gain in children and adults: a systematic review and meta-analysis. *Am J Clin Nutr* **98**, 1084–1102.
15. Stern D, Middaugh N, Rice MS *et al.* (2017) Changes in sugar-sweetened soda consumption, weight, and waist circumference: 2-year cohort of Mexican women. *Am J Public Health* **107**, 1801–1808.
16. Singh GM, Micha R, Khatibzadeh S *et al.* (2015) Global, regional, and national consumption of sugar-sweetened beverages, fruit juices, and milk: a systematic assessment of beverage intake in 187 countries. *PLoS ONE* **10**, e0124845.
17. Fowler SP, Williams K & Hazuda HP (2015) Diet soda intake is associated with long-term increases in waist circumference in a biethnic cohort of older adults: the San Antonio Longitudinal Study of Aging. *J Am Geriatr Soc* **63**, 708–715.
18. van Baak MA & Astrup A (2009) Consumption of sugar and body weight. *Obes Rev* **10**, 15.
19. Vinknes KJ, de Vogel S, Elshorbagy AK *et al.* (2011) Dietary intake of protein is positively associated with percent body fat in middle-aged and older adults. *J Nutr* **141**, 440–446.
20. Rampersaud GC & Valim MF (2017) 100% citrus juice: Nutritional contribution, dietary benefits, and association with anthropometric measures. *Crit Rev Food Sci Nutr* **57**, 129–140.
21. Pan A, Malik VS, Hao T *et al.* (2013) Changes in water and beverage intake and long-term weight changes: results from three prospective cohort studies. *Int J Obes (Lond)* **37**, 1378–1385.
22. Peasey A, Bobak M, Kubinova R *et al.* (2006) Determinants of cardiovascular disease and other non-communicable diseases in Central and Eastern Europe: rationale and design of the HAPIEE study. *BMC Public Health* **6**, 255.
23. Boylan S, Welch A, Pikhart H *et al.* (2009) Dietary habits in three Central and Eastern European countries: the HAPIEE study. *BMC Public Health* **9**, 439.
24. Wuenstel JW, Wądołowska L, Słowińska MA *et al.* (2015) Consumption frequency of fruit juices and sweetened beverages: differences related to age, gender and the prevalence of overweight among polish adolescents. *Pol J Food Nutr Sci.* **65**, 211–221.
25. Khanferyan RA, Radzhabkadiev RM & Evstratova VS (2018) Consumption of carbohydratecontaining beverages and their contribution to the total calorie content of the diet. *Vopr Pitan* **87**, 39–43.
26. O'Neil CE, Nicklas TA, Rampersaud GC *et al.* (2012) 100% Orange juice consumption is associated with better diet quality, improved nutrient adequacy, decreased risk of obesity, and improved biomarkers of health in adults: National Health and Nutrition Examination Survey, 2003-2006. *Nutr J* **11**, 107.
27. Bellisle F, Hébel P, Fourniret A *et al.* (2018) Consumption of 100% pure fruit juice and dietary quality in French adults: analysis of a nationally representative survey in the context of the WHO recommended limitation of free sugars. *Nutrients* **10**, 59.
28. Auerbach BJ, Littman AJ, Krieger J *et al.* (2018) Association of 100% fruit juice consumption and 3-year weight change among postmenopausal women in the in the Women's Health Initiative. *Prev Med* **109**, 8–10.
29. Monsivais P & Rehm CD (2012) Potential nutritional and economic effects of replacing juice with fruit in the diets of children in the United States. *Arch Pediatr Adolesc Med* **166**, 459–464.
30. Luger M, Lafontan M, Bes-Rastrollo M *et al.* (2017) Sugar-Sweetened Beverages and Weight Gain in Children and Adults: A Systematic Review from 2013 to 2015 and a Comparison with Previous Studies. *Obes Facts* **10**, 674–693.
31. Hu FB (2013) Resolved: There is sufficient scientific evidence that decreasing sugar-sweetened beverage consumption will reduce the prevalence of obesity and obesity-related diseases. *Obes Rev* **14**, 606–619.
32. Dimeglio DP & Mattes RD (2000) Liquid versus solid carbohydrate: effects on food intake and body weight. *Int J Obes Relat Metab Disord* **24**, 794–800.
33. Pereira MA (2014) Sugar-Sweetened and Artificially-Sweetened Beverages in relation to obesity risk. *Adv Nutr* **5**, 797–808.
34. World Health Organization (2016). Fiscal policies for diet and prevention of noncommunicable diseases. Geneva: WHO. Available at: http://www.who.int/dietphysicalactivity/publications/fiscal-policies-diet-prevention/en/ (accessed on 16 March 2019).
35. Laverty AA, Magee L, Monteiro CA *et al.* (2015) Sugar and artificially sweetened beverage consumption and adiposity changes: National longitudinal study. *Int J Behav Nutr Phys Act.* **12**, 137.
36. The InterAct consortium (2013) Consumption of sweet beverages and type 2 diabetes incidence in European adults: results from EPIC-InterAct. *Diabetologia* **56**, 1520–1530.
37. Ferreira-Pêgo C, Babio N, Bes-Rastrollo M *et al.* (2016) Frequent consumption of sugar- and artificially sweetened beverages and natural and bottled fruit juices is associated with an increased risk of metabolic syndrome in a Mediterranean population at high cardiovascular disease risk. *J Nutr. Suppl Files* **146**, 1528–1536.
38. Fagherazzi G, Vilier A, Sartorelli DS *et al.* (2013) Consumption of artificially and sugar-sweetened beverages and incident type 2 diabetes in the Etude Epidémiologique auprès des femmes de la Mutuelle Générale de l'Education Nationale-European Prospective

Investigation into Cancer and Nutrition cohort. *Am J Clin Nutr* **97**, 517–523.
39. Fowler SP, Williams K, Resendez RG *et al.* (2008) Fueling the obesity epidemic? artificially sweetened beverage use and long-term weight gain. *Obesity* **16**, 1894–1900.
40. Anton SD, Martin CK, Han H *et al.* (2010) Effects of stevia, aspartame, and sucrose on food intake, satiety, and postprandial glucose and insulin levels. *Appetite* **55**, 37–43.
41. Schulze MB, Manson JE, Ludwig DS *et al.* (2004) Sugar-sweetened beverages, weight gain, and incidence of type 2 diabetes in young and middle-aged women. *JAMA* **292**, 927–934.
42. Prentice RL (2003) Dietary assessment and the reliability of nutritional epidemiology reports. *Lancet* **362**, 182–183.
43. Hansen L, Dragsted OL, Olsen A *et al.* (2010) Fruit and vegetable intake and risk of acute coronary syndrome. *Br J Nutr* **104**, 248–255.
44. Stefler D, Pikhart H, Jankovic N *et al.* (2014) Healthy diet indicator and mortality in Eastern European populations: prospective evidence from the HAPIEE cohort. *Eur J Clin Nutr* **68**, 1346–1352.

Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1. Multivariable logistic regression for body mass index and fruit juice/soft drink consumption by country.

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NUTRITIONAL EPIDEMIOLOGY

Dietary total antioxidant capacity is positively associated with muscular strength in cirrhotic outpatients: a cross-sectional study

L. de Freitas Lima,[1] F. de Faria Ghetti,[1] H. H. M. Hermsdorff,[2] D. G. de Oliveira,[1] G. Teixeira,[3] L. E. V. V.de Castro Ferreira[1] & A. P. B. Moreira[4]

[1]Universitary Hospital and School of Medicine, Universidade Federal Juiz de Fora, Juiz de Fora, Minas Gerais, Brazil
[2]Department of Nutrition and Health, Universidade Federal de Viçosa, Viçosa, Minas Gerais, Brazil
[3]Department of Statistical, Universidade Federal de Viçosa, Viçosa, Minas Gerais, Brazil
[4]Department of Nutrition, Universidade Federal Juiz de Fora, Juiz de Fora, Minas Gerais, Brazil

Keywords
antioxidants, cirrhosis, hand-grip strength, liver, muscular strength.

Correspondence
A. P. B. Moreira, Departamento de Nutrição, Universidade Federal de Juiz de Fora, Bairro Martelos, s/n, CEP 36036-330, Juiz de Fora, Minas Gerais, Brazil.
Tel.: +55 32 21023234
Fax: +55 32 21023215
E-mail: apboroni@yahoo.com.br

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Abstract

Background: Cirrhosis is the end-stage of progressive fibrosis, in which oxidative stress and inflammation-related pathways can modulate the cellular and tissue events involved in the pathogenesis of liver fibrosis. Dietary intake of antioxidants has been suggested to protect against oxidative damage and related clinical complications. The present study aimed to investigate the potential association of the dietary total antioxidant capacity (dTAC) with anthropometric, functional and biochemical markers, as well as the severity of the disease, in cirrhotic outpatients.
Methods: Sixty-two outpatients (38 men and 24 women) with a mean (SD) age of 59.1 (9.9) years were evaluated. Dietary TAC was estimated from a food frequency questionnaire. Aetiology and severity of liver cirrhosis, lifestyle characteristics, occurrence of comorbidities and oedema, and anthropometric, functional and biochemical markers were all assessed.
Results: Cirrhotic outpatients with higher dTAC also had higher values of the hand-grip strength ($P = 0.029$) and arm muscle area ($P = 0.027$). After adjusting by sex, age, smoking and alcohol intake, the addition of 1 mmol day^{-1} of dTAC contributed to increase 0.552 kg f^{-1} in hand-grip strength ($P < 0.05$). The addition of one mmol day^{-1} of dTAC contributed to an arm muscle area increase 0.565 cm^2 ($P < 0.05$) on average.
Conclusions: The dTAC was positively associated with hand-grip strength and arm muscle area in cirrhotic outpatients. The implications of the present study are important in clinical practice because a diet rich in antioxidants may be an ally in the control of excessive reactive oxygen species production in cirrhotic outpatients with repercussion on muscle mass and strength.

Introduction

Cirrhosis is the end-stage of progressive fibrosis, in which oxidative stress and inflammation-related pathways can modulate the cellular and tissue events involved in the pathogenesis of liver fibrosis [(1)]. In this sense, oxidative stress causes liver damage by changes in DNA, proteins and lipids, as well as modulation of biological pathways associated with gene transcription, protein expression, cellular apoptosis and activation of hepatic stellate cells [(2)]. Moreover, inflammation is an essential component of the immune response and manifests as infiltration of inflammatory cells, mainly in the liver, in the fight against invasion of pathogens. The persistence of inflammatory

stimuli and oxidative stress can lead to cellular damage and lipid accumulation, associated with an increased risk of steatohepatitis, fibrosis and cancer [2–4].

In turn, several studies have demonstrated the role of diet in modulate inflammation [5,6] and oxidative stress [7]. Foods and bioactive compounds (such as coffee, green tea, resveratrol, curcumin, quercetin, silymarin, naringenin) have been considered beneficial to liver diseases [8–11].

In this context, the total antioxidant capacity of foods, which describes the combined ability of dietary antioxidants to eliminate preformed free radicals, has been suggested as a tool to investigate the health effects of antioxidants in mixed diets [12–14]. Our previous study involving non-alcoholic steatohepatitis (NASH) showed a negative association between dietary total antioxidant capacity (dTAC) and hepatic injury (ballooning) [15], although investigations of dTAC in cirrhotic outpatients have yet not been reported in the literature yet. Frequently patients with cirrhosis present alterations in specific aspects of nutritional status, such as micronutrient deficiencies and/or global malnutrition (e.g. as a result of poor nutritional intake). The provision of the necessary nutrients must compensate for these existing deficiencies [16–18]. Thus, the present study aimed to investigate the potential association of dTAC with anthropometric, functional and biochemical markers, as well as cirrhosis severity, in outpatients.

Materials and methods

Study design

This cross-sectional study was conducted in the Hepatology Service of the University Hospital at the Federal University of Juiz de Fora, Minas Gerais, Brazil. Approximately 78 outpatients with cirrhosis are attended monthly. The study was conducted from May to December 2017. The inclusion criteria were outpatients with liver cirrhosis over 18 years of age, of both sexes, who were followed up on an outpatient basis during the study period. Patients with cancer, autoimmune diseases (systemic lupus erythematosus, rheumatoid arthritis), previous renal insufficiency and presence of hepatic encephalopathy or other physical or mental condition that compromised the interview process and/or anthropometric and functional evaluation were not included. Patients who underwent liver transplantation or who were awaiting transplantation were also excluded. The subjects were taken into the study after they provided their written informed consent. This study was conducted in accordance with the Declaration of Helsinki. All procedures involving human subjects/patients were approved by the Ethics Committee of the Federal University of Juiz de Fora (protocol number 1.129.516/2015) and all participants provided written informed consent.

Data collection

Information on age, sex, alcohol, smoking and food consumption was obtained from face-to-face interviews. On the same day of the interview, the anthropometric and functional data were collected.

Cirrhosis severity

Aetiology and cirrhosis severity, presence of comorbidities, oedema and biochemical data were obtained from medical records. The diagnosis of cirrhosis was based on clinical, laboratory, imaging and/or histopathological evaluation, according to the routine of the Hepatology Service. Child–Turcotte–Pugh (CTP) was used to assess the cirrhosis severity [19,20], where variables such as ascites, encephalopathy, time of prothrombin, bilirubin and albumin were graduated in scores of 1 and 3 points each. The final sum made it possible to classify the patients in degrees of severity A or B. It should be emphasised that, as a result of the inclusion criteria, no patients were classified as severity grade C because the occurrence of hepatic encephalopathy, common in this class of patients, is associated with some degree of mental confusion and this factor could compromise the completion of the questionnaires.

Biochemical measurements

The biochemical data originated from medical records. As a routine of the Hepatology Service, blood collection was performed after a 12-h fast. The blood was separated by centrifugation and immediately analysed in the Laboratory of Clinical Analyses of the University Hospital. Hemoglobin, leukocytes, platelets, mean corpuscular volume, mean corpuscular hemoglobin concentration, aspartate aminotransferase, alanine amino transferase, alkaline phosphatase, gammaglutamyl transferase, urea, creatinine, potassium, albumin, and total bilirubin were determined using standard laboratory methods in an autoanalyser (model CT600i; Wiener Lab, Rosario, Argentina).

Anthropometric and functional evaluation

The arm circumference (AC) was measured at the midpoint between the acromial process and the olecranon process, using a flexible and inelastic measuring tape. Biceps skinfold (BSF) and triceps skinfold (TSF) were measured using an adipometer (Lange Skinfold Caliper; Lange, Houston, TX, USA). The arm muscle area (AMA) was calculated from the values obtained from TSF and AC.

Functional assessment was performed using hand-grip strength (HSG) and adductor pollicis muscle thickness (APMT). The measurement of HSG was performed using a Jamar hydraulic hand dynamometer (Sammons Preston Rolyan, Chicago, IL, USA). Patients remained seated with their elbows supported and flexed at a 90° angle, performing the greatest possible strength with the dominant hand. Three trials were performed with a 1-min rest interval between the measurements and the largest of the three was used in the analysis. The APMT measurement was performed with the patient seated, the arm flexed at a 90° angle with the forearm and the hand resting on the knee. The adductor muscle was pinched at the apex of an imaginary triangle formed by the extension of the thumb and forefinger.

Estimation of dietary total antioxidant capacity

The habitual diet was obtained through a food frequency questionnaire previously validated by Mannato *et al.* [21]. Daily food consumption was estimated as frequency versus portion size for each item consumed. All food questionnaires were analysed by the same nutritionist. For the determination of dTAC, a previously published database [22] was used, combined with the supporting literature [23–30], using the ferric reducing ability of plasma (FRAP) method with a calibration curve made with ferrous sulfate, for the TAC determination of food. Intake evaluation was performed using a standard spreadsheet developed in EXCEL (Microsoft Corp., Redmond, WA, USA) by adding individual TAC values from the FRAP assay of each food and expressed as TAC in mmol day^{-1}. To assign a TAC value to foods not available in the articles and in the database, botanically similar food data were used. When TAC values for cooked foods were not available, TAC levels of fresh foods were considered for estimation purposes. Total dTAC was the sum of dTAC of all consumed foods.

Statistical analysis

The normality of the data was determined by the Shapiro–Wilk test. Comparisons of continuous variables were conducted using the parametric Student's *t*-test or nonparametric Mann–Whitney *U* test. Categorical variables were compared using the chi-squared test. To determine the influence of dTAC, outpatients were divided into two groups according to the median dTAC value (10.5 mmol day^{-1}): lower and higher/equal dTAC. A multiple linear regression model was used to verify the association of dTAC with HSG and AMA measurements. This model was controlled by sex, age, smoking status and alcohol intake. A scatter plot was built to illustrate the association. The contribution of each food group to the dTAC was calculated as the ratio of the antioxidant intake from that food group to the total intake from all foods. Data are presented as the mean (SD), or median and minimum and maximum. Categorical variables are expressed as relative (%) and absolute (*n*) frequencies. All statistical analyses were performed using SPSS, version 20.0 (IBM Corp., Armonk, NY, USA). $P < 0.05$ was considered statistically significant.

Results

During the study period, 458 outpatients were followed up at the Hepatology Service. Of these patients, 111 were not cirrhotic. Among 347 patients with cirrhosis, 50 did not agree to participate in the study, 37 were not able to answer the questionnaires, 44 had hepatocellular carcinoma, 31 were awaiting liver transplantation and 123 were excluded for various reasons (incomplete medical records, presence of others cancers, autoimmune diseases and chronic kidney disease). Thus, 62 outpatients were included in our analyses. These outpatients had a mean (SD) age of 59.1 (9.9) years and a demonstrated a predominance of males 61.3% ($n = 38$).

Among the cirrhosis patients, the majority (37.1%; $n = 23$) were of alcoholic origin, followed by hepatitis C infection (33.9%; $n = 21$), NASH (20.9%; $n = 13$) and other causes such as autoimmune hepatitis or undefined causes (8.1%; $n = 5$). The most common comorbidities observed in these outpatients were hypertension (53.2%; $n = 33$), diabetes (45.2%; $n = 28$), coronary diseases (16.1%; $n = 10$) and hypothyroidism (12.9%; $n = 8$). The CTP classification revealed that 45 outpatients (72.6%) were class A and 17 (27.4%) were class B. The presence of oedema (ascites and lower limb oedema) could be considered to be a complication of cirrhosis and was present in 37.1% ($n = 23$) of the outpatients evaluated.

Regarding the characteristics related to the lifestyle of the outpatients, 16.1% ($n = 10$) were smokers. Alcohol consumption was present in 8.1% ($n = 5$) of outpatients, even after receiving medical advice to abolish alcohol consumption because of its deleterious role in liver function. The anthropometric/functional data, biochemical markers and cirrhosis severity (Tables 1–3) were compared from the median value of the dTAC (10.5 mmol day^{-1}). Outpatients who had a higher dTAC also presented higher values for HSG ($P = 0.029$) and AMA ($P = 0.027$). The other anthropometric/functional, biochemical and disease severity measures did not differ between the groups.

When we performed a multiple linear regression, the adjusted model indicated that the addition of one mmol day^{-1} of dTAC contributed to increase 0.552 kg f^{-1} in HSG ($P < 0.05$). The model adjusted by dTAC, sex and

Table 1 Anthropometric and functional data according to dietary total antioxidant capacity (dTAC) in cirrhotic outpatients

	dTAC < 10.5 mmol day^{-1} (n = 31)	dTAC ≥ 10.5 mmol day^{-1} (n = 31)	P-values
AC (cm)	30.8 (4.8)	32.8 (3.3)	0.053
BSF (mm)	29.3 (12.6)	31.4 (10.2)	0.488
TSF (mm)	20.5 (11.7)	22.2 (10.4)	0.530
AMA (cm^2)	36.8 (8.8)	42.3 (10.2)	**0.027**
HSG (kg f^{-1})	19.0 (5.0–42.0)	31.0 (10.0–48.0)	**0.029***
APMT (mm)	10.4 (4.0–24)	11.0 (4.0–19.0)	0.657*

AC, arm circumference; AMA, arm muscle area; APMT, adductor pollicis muscle thickness; BSF, biceps skinfold; HSG, hand-grip strength; TSF, triceps skinfold.
Continuous variables are given as the mean (SD) or median (minimum–maximum).
Student's t-test or Mann–Whitney U test (*). $P < 0.05$ was considered statistically significant (bold values).

Table 2 Biochemical markers according to dietary total antioxidant capacity (dTAC) in cirrhotic outpatients

	dTAC < 10.5 mmol day^{-1} (n = 31)	dTAC ≥ 10.5 mmol day^{-1} (n = 31)	P-values
Haemoglobin (g dL^{-1})	13.2 (1.9)	13.1 (1.9)	0.999
Leukocytes (mm^3)	5184.3 (2124.6)	4729.4 (2152.8)	0.414
Platelets (mm^3)	113994.8 (63287.9)	96478.7 (40964.0)	0.201
MCV (fl)	94.2 (8.7)	91.4 (7.2)	0.196
MCHC (g dL^{-1})	33.0 (28.0–35.0)	33.0 (28–38.0)	0.482*
AST (U L^{-1})	36.0 (21.0–140.0)	35.0 (18.0–202.0)	0.762*
ALT (U L^{-1})	30.6 (21.2)	38.0 (35.5)	0.352
AP (U L^{-1})	247.0 (164.5)	241.8 (196.3)	0.914
GGT (U L^{-1})	85.0 (22.0–481.0)	59.0 (17.0–711.0)	0.555*
Urea (mg dL^{-1})	34.0 (17.0)	39.6 (31.7)	0.482
Creatinine (mg dL^{-1})	1.0 (0.0–2.0)	1.0 (0.0–5.0)	0.407*
Potassium (mEq L^{-1})	4.0 (4.0–6.0)	4.0 (4.0–6.0)	0.542*
Albumin (g dL^{-1})	4.0 (2.0–4.0)	4.0 (3.0–5.0)	0.175*
Total bilirubin (mg dL^{-1})	1.0 (0.0–5.0)	1.0 (0.0–5.0)	0.824*

ALT, alanine amino transferase; AP, alkaline phosphatase; AST, aspartate aminotransferase; GGT, gamma glutamyl transferase; MCHC, mean corpuscular hemoglobin concentration; MCV, mean corpuscular volume.
Continuous variables are given as the mean (SD) or median (minimum–maximum).
Student's t-test or Mann–Whitney U test (*). $P < 0.05$ was considered statistically significant.

Table 3 Cirrhosis severity according to dietary total antioxidant capacity (dTAC)

Variable	dTAC < 10.5 mmol dia^{-1} (n = 31)	dTAC ≥ 10.5 mmol dia^{-1} (n = 31)	P-value*
CTP A	66.7% (21)	77.4% (24)	0.393
CTP B	32.3% (10)	22.6% (7)	

CTP, Child–Turcotte–Pugh.
Nominal variables are given as the number of outpatients with the characteristic of interest.
*Chi-squared test. $P < 0.05$ was considered statistically significant.

age is able to explain 52.7% of the HSG variation. There was no significant difference between smokers and non-smokers, as well as among those who drank alcoholic or non-alcoholic beverages. With regard to AMA, the addition of one mmol day^{-1} of dTAC contributed to an increase of 0.565 cm^2 in this nutritional marker ($P < 0.05$). The model adjusted by dTAC and sex is able to explain 36.3% of AMA variation, regardless of age, smoking habit or drinking alcoholic beverage (Fig. 1).

Coffee and tea, fruits and fruit juices, vegetables, and legumes were the major food or food groups of dTAC (49.5%, 20.4%, 4.1% and 3.3%, respectively).

Discussion

The intake of dietary antioxidants appears to protect against oxidative damage and related clinical complications [13,15,31,32]. To our knowledge, this is the first study to evaluate dTAC in cirrhotic outpatients, with the main finding being a positive association between dTAC and muscular strength.

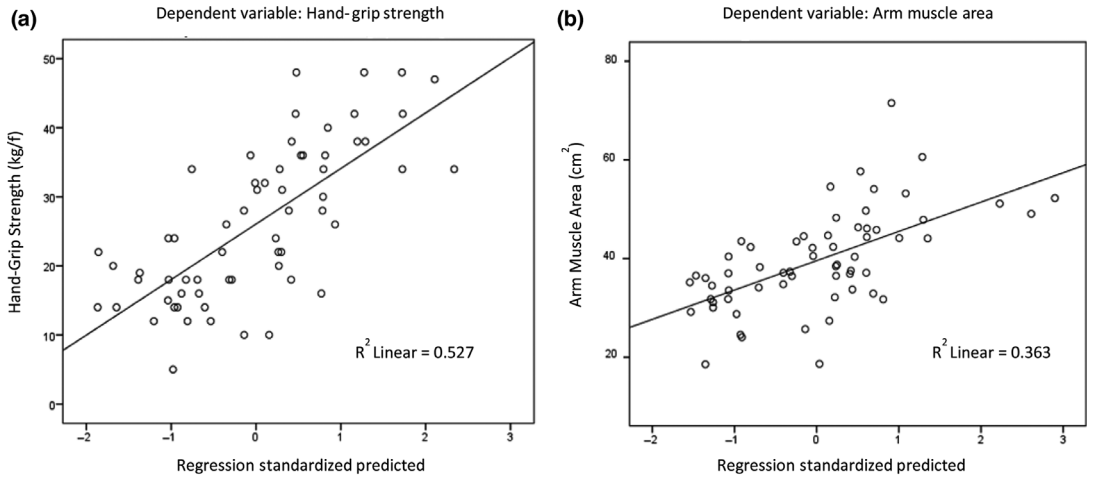

Figure 1 Association between observed values of hand-grip strength (a) and arm muscle area (b) versus predicted values by the adjusted model (dietary total antioxidant capacity, age, sex, smoking, and alcohol intake) in cirrhotic outpatients.

Underlying the pathogenesis of chronic disease is the state of oxidative stress [33]. Oxidative stress is also present in skeletal muscle wasting [34], being a complicating factor of liver diseases and ageing [35,36]. The main oxidant types are reactive oxygen species (ROS). Oxidative stress has been functionally linked to muscle wasting through ubiquitin–proteasome system activation, where increased ROS activates proteasome-dependent protein degradation. Another consequence of oxidative stress is oxidative damage generated in the cell, as indicated by protein and lipid oxidation [35]. Indeed, studies have confirmed increased markers of oxidative stress in sarcopaenic individuals [37,38].

Sarcopaenia is a syndrome characterised by progressive and widespread loss of skeletal muscle mass, strength and function [36]. The potential impact of sarcopaenia is great, considering that muscle tissue is the most abundant in the human body [39]. In cirrhosis, the presence of sarcopaenia should be assessed because sarcopaenia is a strong predictor of mortality and morbidity [16,17]. The prevalence of sarcopaenia in patients with hepatic cirrhosis ranges from 40% to 70% [40,41] and is favoured by the combination of cofactors such as advanced age associated with interference of the degree of liver disease in the nutritional status of this population [42]. In addition, chronic alcohol consumption is also associated with sarcopaenia because ROS generated during ethanol metabolism can damage many tissues, including liver and skeletal muscle [33]. Studies confirm that patients with liver disease as a result of chronic alcohol abuse have a marked inflammation and an oxidative imbalance with elevated malondialdehyde (oxidative stress marker) and reduced and oxidised glutathione (antioxidant function) [43,44]. It should be noted that, in the present study, the main cause of cirrhosis was alcohol consumption.

Patients with cirrhosis may develop simultaneous loss of skeletal muscle and gain of adipose tissue, culminating in a condition called 'sarcopaenic obesity' [17]. Still, muscle depletion is characterised by both reduced muscle size and increased proportion of intermuscular and intramuscular fat, termed myosteatosis [45]. Given the great difficulty of evaluating the nutritional status of cirrhotic patients in clinical practice, in the present study, we chose not to evaluate body mass index. More than 37% of the outpatients presented oedema, which could mask the body weight and overestimate the excess weight. However, the BSF and TSF values, which reflect subcutaneous adipose tissue, were above the expected value for the 50th percentile [46]. It should be noted that these two skin folds were not influenced by water retention in our outpatients (ascites and oedema of the lower limbs).

The diagnostic criteria for sarcopaenia in cirrhosis have not been firmly established so far. Currently, an approach based on mass assessment (dual X-ray absorptiometry or computed tomography), muscular strength and/or function (gait speed or chair stand test) can be recommended. The reduction of muscular strength can be evaluated by HSG (general muscular strength indicator, with cut-off points: <20 kg f^{-1} (women) and <30 kg f^{-1} (men) [36].

Our data demonstrate a relationship between dTAC versus AMA and HSG in cirrhotic outpatients, suggesting a possible role of antioxidant intake in muscle mass and strength. Indeed, studies have shown the relationship between antioxidants and muscle mass. Kim *et al.* [47], for example, observed a beneficial effect on muscle mass and physical function measured by the ability to walk in elderly sarcopaenic women from catechin

supplementation (strong antioxidant action) associated with physical exercise. Chung *et al.* [48] found that consumption of at least three cups of coffee day^{-1} was associated with a lower prevalence of sarcopaenia in elderly men. Another study demonstrated an anabolic role of resveratrol in exercise-induced adaptations in older men and women [49]. Thus, to reduce the production of free radicals and to attenuate oxidative stress with possible impact on muscle mass and strength, it is recommended to increase the consumption of foods with higher antioxidant capacity, such as coffee, tea, fruits, vegetables and legumes [13,29,50,51]. In the present study, coffee/tea and fruits were the main contributors to dTAC, which is not surprising considering our previous results involving patients with NASH [15] and those of Torres and Farah [52] with the Brazilian diet. Because foods contain many different types of antioxidants (vitamins, carotenoids, polyphenols and other bioactive compounds as yet unknown), TAC has been suggested as a more appropriate tool for investigating the relationship between the antioxidant potential of the diet and the diseases/clinical complications related to oxidative stress. It is important to note that current guidelines on nutrition in liver disease reinforce the need for additional data on the efficacy of antioxidant use in patients with liver disease.

Changes in muscle function/strength may be detected earlier than changes in laboratory parameters [53], which may partly explain the lack of a relationship of dTAC with biochemical data and severity of liver disease.

A strength of the present study was the inclusion of more homogeneous cirrhotic outpatients (all were CTP class A or B only and were also in outpatient follow-up). Limitations of the present study include a cross-sectional design that does not allow the evaluation of temporal relationships and the absence of imaging tests and tests to verify muscle function with respect to evaluating sarcopaenia.

In conclusion, the dTAC is associated with better parameters related to muscle mass and strength in cirrhotic outpatients, which may be a result of its assumed role with respect to reducing ROS or improving the quality of the diet in general. More studies are needed to address the consumption of foods with antioxidant potential over the long term to confirm our findings and to evaluate the benefit of food interventions in cirrhosis, as well as its clinical complications.

Conflict of interests, source of funding and authorship

The authors declare that they have no conflicts of interest.

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LFL, APBM, FFG and LEVVCF contributed to the conception and design of the study. LFL and DGO contributed to the data collection. HHMF participated in the evaluation of the dietary total antioxidant capacity. GL and DGO carried out data analysis and interpretation. LFL and APBM performed the first draft of the article. All authors critically reviewed the manuscript and approved the final version submitted for publication.

Transparency declaration

The lead author affirms that this manuscript is an honest, accurate and transparent account of the study being reported. The reporting of this work is compliant with STROBE guidelines. The lead author affirms that no important aspects of the study have been omitted and that any discrepancies from the study as planned have been explained.

References

1. Sánches-Valle V, Chávez-Tapia NC, Uribe M *et al.* (2012) Role of oxidative stress and molecular changes in liver fibrosis: a review. *Curr Med Chem* **19**, 4850–4860.
2. Li S, Hong M, Tan HY *et al.* (2016) Insights into the role and interdependence of oxidative stress and inflammation in liver diseases. *Oxid Med Cell Longev* **2016**, 4234061.
3. Robinson MW, Harmon C & O'Farrelly C (2016) Liver immunology and its role in inflammation and homeostasis. *Cell Mol Immunol* **13**, 267–276.
4. Seki E & Schwabe RF (2015) Hepatic inflammation and fibrosis: functional links and key pathways. *Hepatology* **61**, 1066–1079.
5. Silveira BKS, Oliveira TMS, Andrade PA *et al.* (2018) Dietary pattern and macronutrients profile on the variation of inflammatory biomarkers scientific update. *Cardiol Res Pract* **2018**, 4762575.
6. Rocha DMUP, Lopes LL, da Silva A *et al.* (2017) Orange juice modulates proinflammatory cytokines after high-fat saturated meal consumption. *Food Funct* **8**, 4396–4403.
7. Cocate PG, Natali AJ, Alfenas RC *et al.* (2015) Carotenoid consumption is related to lower lipid oxidation and DNA damage in middle-aged men. *Br J Nutr* **114**, 257–264.
8. Arrigo T, Leonardi S, Cuppari C *et al.* (2015) Role of the diet as a link between oxidative stress and liver diseases. *World J Gastroenterol* **21**, 384–395.

9. Casas-Grajales S & Muriel P (2015) Antioxidants in liver health. *World J Gastrointest Pharmacol Ther* **6**, 59–72.
10. Arauz J, Moreno MG, Cortés-Reynosa P *et al.* (2013) Coffee attenuates fibrosis by decreasing the expression of TGF-β and CTGF in a murine model of liver damage. *J Appl Toxicol* **33**, 970–979.
11. Halegoua-De Marzio D, Kraft WK, Daskalakis C *et al.* (2012) Limited sampling estimates of epigallocatechin gallate exposures in cirrhotic and noncirrhotic patients with hepatitis C after single oral doses of green tea extract. *Clin Ther* **34**, 2279–2285.
12. Wang Y, Yang M, Lee SG *et al.* (2012) Dietary total antioxidant capacity is associated with diet and plasma antioxidant status in healthy young adults. *J Acad Nutr Diet* **112**, 1626–1635.
13. Puchau B, Zulet MA, De Echávarri AG *et al.* (2010) Dietary total antioxidant capacity is negatively associated with some metabolic syndrome features in healthy young adults. *Nutrition* **26**, 534–541.
14. Valtueña S, Pellegrini N, Franzini L *et al.* (2008) Food selection based on total antioxidant capacity can modify antioxidant intake, systemic inflammation, and liver function without altering markers of oxidative stress. *Am J Clin Nutr* **87**, 1290–1297.
15. Oliveira DG, Ghetti FF, Moreira APB *et al.* (2018) Association between dietary total antioxidant capacity and hepatocellular ballooning in nonalcoholic steatohepatitis: a cross-sectional study. *Eur J Nutr* Jul 17. https://doi.org/10.1007/s00394-018-1776-0. [Epub ahead of print].
16. Plauth M, Bernal W, Dasarathy S *et al.* (2019) ESPEN guideline on clinical nutrition in liver disease. *Clin Nutr* **38**, 485–521.
17. European Association for the Study of the Liver (2019) EASL clinical practice guidelines on nutrition in chronic liver disease. *J Hepatol* **70**, 172–193.
18. McClain CJ (2016) Nutrition in patients with cirrhosis. *Gastroenterol Hepatol (NY)* **12**, 507–510.
19. Child CG & Turcotte JG (1964) Surgery and portal hypertension. *Major Probl Clin Surg* **1**, 1–85.
20. Pugh RN, Murray-Lyon IM, Dawson JL *et al.* (1973) Transection of the oesophagus for bleeding oesophageal varices. *Br J Surg* **60**, 646–649.
21. Mannato LW, Pereira TS, Velasquez-Melendez G *et al.* (2015) Comparison of a short version of the Food Frequency Questionnaire with its long version – a cross-sectional analysis in the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil). *São Paulo Med J* **133**, 414–420.
22. Carlsen MH, Halvorsen BL, Holte K *et al.* (2010) The total antioxidant content of more than 3100 foods, beverages, spices, herbs and supplements used worldwide. *Nutr J* **9**, 3.
23. Payne AC, Mazzer A, Clarkson GJ *et al.* (2013) Antioxidant assays – consistent findings from FRAP and ORAC reveal a negative impact of organic cultivation on antioxidant potential in spinach but not watercress or rocket leaves. *Food Sci Nutr* **1**, 439–444.
24. Tiveron AP, Melo OS, Bergamaschi KB *et al.* (2012) Antioxidant activity of Brazilian vegetables and its relation with phenolic composition. *Int J Mol Sci* **13**, 8943–8957.
25. Halvorsen BL & Blomhoff R (2011) Validation of a quantitative assay for the total content of lipophilic and hydrophilic antioxidants in foods. *Food Chem* **127**, 761–776.
26. Paśko P, Bartoń H, Fołta M *et al.* (2007) Evaluation of antioxidant activity of amaranth (*Amaranthus cruentus*) grain and by-products (flour, popping, cereal). *Rocz Panstw Zakl Hig* **58**, 35–40.
27. Halvorsen BL, Carlsen MH, Phillips KM *et al.* (2006) Content of redox-active compounds (ie, antioxidants) in foods consumed in the United States. *Am J Clin Nutr* **84**, 95–135.
28. Llorach R, Tomás-Barberán FA & Ferreres F (2004) Lettuce and chicory byproducts as a source of antioxidant phenolic extracts. *J Agric Food Chem* **52**, 5109–5116.
29. Pellegrini N, Serafini M, Colombi B *et al.* (2003) Total antioxidant capacity of plant foods, beverages and oils consumed in Italy assessed by three different in vitro assays. *J Nutr* **133**, 2812–2819.
30. Halvorsen BL, Holte K, Myhrstad MC *et al.* (2002) A systematic screening of total antioxidants in dietary plants. *J Nutr* **132**, 461–471.
31. Hermsdorff HHM, Puchau B, Volp ACP *et al.* (2011) Dietary total antioxidant capacity is inversely related to central adiposity as well as to metabolic and oxidative stress markers in healthy young adults. *Nutr Metab (Lond)* **8**, 59.
32. Hermsdorff HHM, Barbosa KBF, Volp ACP *et al.* (2012) Vitamin C and fibre consumption from fruits and vegetables improves oxidative stress markers in healthy young adults. *Br J Nutr* **107**, 1119–1127.
33. Moylan JS & Reid MB (2007) Oxidative stress, chronic disease, and muscle wasting. *Muscle Nerve* **b35**, 411–429.
34. Semba RD, Lauretani F & Ferrucci L (2007) Carotenoids as protection against sarcopenia in older adults. *Arch Biochem Biophys* **458**, 141–145.
35. Campos F, Abrigo J, Aguirre J *et al.* (2018) Sarcopenia in a mice model of chronic liver disease: role of the ubiquitin-proteasome system and oxidative stress. *Pflugers Arch* **470**, 1503–1519.
36. Anand AC (2017) Nutrition and muscle in cirrhosis. *J Clin Exp Hepatol* **7**, 340–357.
37. Bellanti F, Romano AD, Lo Buglio A *et al.* (2018) Oxidative stress is increased in sarcopenia and associated with cardiovascular disease risk in sarcopenic obesity. *Maturitas* **109**, 6–12.
38. Zacarías-Flores M, Sánches-Rodríguez MA, García-Anaya OD *et al.* (2018) Relationship between oxidative stress and muscle mass loss in early postmenopause: an exploratory study. *Endocrinol Diabetes Nutr* **65**, 328–334.

39. Leite LEA, Resende TL, Nogueira GM *et al.* (2012) Aging, oxidative stress and sarcopenia: a systemic approach. *Rev Bras Geriatr Gerontol* **15**, 365–380.
40. Kim HY & Jang JW (2015) Sarcopenia in the prognosis of cirrhosis: going beyond the MELD score. *World J Gastroenterol* **21**, 7637–7647.
41. Aby ES, Lee E, Saggi SS et al. (2018) Pretransplant sarcopenia in patients with NASH cirrhosis does not impact rehospitalization or mortality. *J Clin Gastroenterol* Sep 1. https://doi.org/10.1097/mcg.0000000000001109. [Epub ahead of print].
42. Dasarathy S (2012) Consilience in sarcopenia of cirrhosis. *J Cachexia Sarcopenia Muscle* **3**, 225–237.
43. Galicia-Moreno M, Rosique-Oramas D, Medina-Avila Z *et al.* (2016) Behavior of oxidative stress markers in alcoholic liver cirrhosis patients. *Oxid Med Cell Longev* **2016**, 9370565.
44. Singh M, Gupta S, Singhal U *et al.* (2013) Evaluation of the oxidative stress in chronic alcoholics. *J Clin Diagn Res* **7**, 1568–1571.
45. Thandassery RB & Montano-Loza AJ (2016) Role of nutrition and muscle in cirrhosis. *Curr Treat Options Gastroenterol* **14**, 257–273.
46. Frisancho AR (1981) New norms of upper limb fat and muscle areas for assessment of nutritional status. *Am J Clin Nutr* **34**, 2540–2545.
47. Kim H, Suzuki T, Saito K *et al.* (2013) Effects of exercise and tea catechins on muscle mass, strength and walking ability in community-dwelling elderly Japanese sarcopenic women: a randomized controlled trial. *Geriatr Gerontol Int* **13**, 458–465.
48. Chung H, Moon JH, Kim JI *et al.* (2017) Association of coffee consumption with sarcopenia in Korean elderly men: analysis using the Korea National Health and Nutrition Examination Survey, 2008–2011. *Korean J Fam Med* **38**, 141–147.
49. Alway SE, McCrory JL, Kearcher K *et al.* (2017) Resveratrol enhances exercise-induced cellular and functional adaptations of skeletal musclein older men and women. *J Gerontol A Biol Med Sci* **72**, 1595–1606.
50. Micek A, Grosso G, Polak M *et al.* (2018) Association between tea and coffee consumption and prevalence of metabolic syndrome in Poland – results from the WOBASZ II study (2013–2014). *Int J Food Sci Nutr* **69**, 358–368.
51. Agudo A, Cabrera L, Amiano P *et al.* (2007) Fruit and vegetable intakes, dietary antioxidant nutrients, and total mortality in Spanish adults: findings from the Spanish cohort of the European Prospective Investigation into Cancer and Nutrition (EPIC-Spain). *Am J Clin Nutr* **85**, 1634–1642.
52. Torres T & Farah A (2017) Coffee, maté, açaí and beans are the main contributors to the antioxidant capacity of Brazilian's diet. *Eur J Nutr* **56**, 1523–1533.
53. Jeejeebhoy KN (1998) Nutritional assessment. *Gastroenterol Clin North Am* **27**, 347–369.

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NUTRITIONAL EPIDEMIOLOGY

Impact of different exercise training modalities on energy and nutrient intake and food consumption in sedentary middle-aged adults: a randomised controlled trial

L. Jurado-Fasoli[1] F. J. Amaro-Gahete[1,2] A. De-la-O[1] & M. J. Castillo[1]

[1]Departament of Medical Physiology, School of Medicine, University of Granada, Granada, Spain
[2]PROmoting FITness and Health through Physical Activity Research Group (PROFITH), Department of Physical Education and Sports, Faculty of Sport Sciences, University of Granada, Granada, Spain

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Correspondence
L. Jurado-Fasoli and F. J. Amaro-Gahete, Department of Medical Physiology, University of Granada, Av. Investigation 11, 18016 Granada, Spain.
Tel.: +34 958243540
Fax: +34 958246179
E-mails: juradofasoli@ugr.es (LJ-F) and amarof@ugr.es (FJA-G)

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Abstract

Background: Exercise could influence energy and macronutrient intake, which could have an important role on body composition changes in response to exercise. The present study aimed to investigate the effects of different training modalities in energy and macronutrient intake, and whether changes in energy and macronutrient intake influences changes in body composition in response to different training modalities.
Methods: A 12-week randomised controlled trial was conducted. Eighty middle-aged sedentary adults were randomised to: (i) a control group; (ii) physical activity recommendation from the World Health Organization; (iii) high-intensity interval training; and (iv) whole-body electromyostimulation training. Dietary intake was assessed using the average of three 24-h recalls.
Results: High-intensity interval training and whole-body electromyostimulation training groups showed lower fibre intake and higher dietary energy density. Our results showed a negative association was found between changes in energy intake and changes in lean mass index. No association was found between changes in protein intake and changes in lean mass index.
Conclusions: In conclusion, we observed a higher dietary energy density and lower fibre intake in high-intensity training groups.

Introduction

The prevalence of being overweight and obesity has increased substantially in all societies across the globe during the last three decades, becoming a major public health concern as a result of its negative effects on health status [(1)]. If trends continue, by 2030, an estimated 38% of the world's adult population will be overweight and another 20% will be obese [(2)]. Obesity increases the risk of chronic diseases (i.e. type 2 diabetes, cardiovascular disease, certain types of cancers) and mortality [(1,2)].

Diet, exercise and behavior modifications are the cornerstones of obesity prevention and treatment [(3)]. Physical exercise produces an energy deficit through increased energy expenditure that may help to reduce overweight and obesity [(1)]. Additionally, it is well-known that exercise is related to improvements in the restoration of the lipid profile, improvements of the autonomic nervous activity and haemodynamic function, improvements of body composition, and an increase in metabolic activity [(4)].

The second cornerstone of obesity treatment is diet modification. Several dietary strategies have been

demonstrated to be effective with respect to reducing body weight, and also for attenuating the presence of comorbid risk factors [5]. These dietary strategies include: (i) reducing portion sizes; (ii) using meal replacement products to reduce dietary choice and caloric intake; (iii) choosing more nutrient-dense and less energy-dense foods; and (iv) altering macronutrient composition, glycaemic index/load, meal frequency, or eating pattern [5].

The weight loss in exercise training programmes is usually less than predicted. This observation could be the result of a compensatory increase in calorie consumption, changes in specific food intakes and/or decreased non-exercise activity thermogenesis [6]. Acute exercise can suppress subjective appetite ratings, subsequent energy intake and alter appetite-regulating hormones for a period of time post-exercise [7]. However, the literature is mixed in terms of exercise training. A recent meta-analysis did not find consistent evidence that exercise training effects energy or macronutrient intake [8]. By contrast, Hopkins *et al.* [9] reported that compensatory responses to an exercise programme of 12 weeks in duration showed a large inter-individual variability.

Two novel training methods comprising high-intensity interval training (HIIT) and whole-body electromyostimulation (WB-EMS) have demonstrated to improved body composition [10,11], although no studies have investigated whether dietary modifications occur in response to these training modalities.

The majority of studies have focused on acute or mid-length, rather than long-term, effects of exercise in energy and nutrient intake. Furthermore, most of these studies have concentrated on a single exercise modality, without comparing different training modalities. Although exercise modality, intensity and duration could influence the intake regulation in different ways, it is still unknown whether a novel training modality such as WB-EMS training could influence dietary intake.

We hypothesise that different training modalities with different intensities and duration could modulate energy and macronutrient intake. Subsequently, changes in body composition could be modulated by changes in energy intake during the training programme. Therefore, the present study aimed to investigate the effects of different training modalities on energy and macronutrient intake in sedentary middle-aged adults. Additionally, we also investigated whether changes in energy and macronutrient intake influences changes in body composition in response to different exercise training programmes.

Materials and methods

Participants

Between April 2015 and December 2016, 141 adults aged 45–65 years were screened in the FIT-AGEING study, an exercise-based randomised controlled trial (clinicaltrial.gov: ID: NCT03334357) [12]. Figure 1 shows the flow of participants from recruitment to follow-up.

The participants were recruited from the province of Granada (Spain) using social networks, local media and posters. Interested individuals were screened via telephone and/or e-mail. Inclusion criteria were to be sedentary (<20 min of moderate-intensity physical activity on 3 days week^{-1} over the last 3 months) and to have a stable weight over the last 6 months. All participants needed to be free of disease, not pregnant or lactating. The study was approved by the Ethics Committee on Human Research at the University of Granada and 'Servicio Andaluz de Salud' (CEI-Granada) [0838-N-2017) and all participants provided their written informed consent. The study protocols and experimental design were applied in accordance with the last revised ethical guidelines of the Declaration of Helsinki. All of the baseline and follow-up examinations were performed at the same setting (Instituto Mixto Universitario Deporte y Salud at the University of Granada).

Study design

A 12-week randomised control trial was conducted with a parallel group design in accordance with the Consolidated Standards of Reporting Trials guidelines (Table S1) [13]. The study was performed between the months of September and December. After completing the baseline measurements, the participants were randomised using a computer-generated simple randomisation [14] to four different groups: (i) control group (no exercise); (ii) physical activity recommendation from the World Health Organization (PAR) group; (iii) HIIT group; and (iv) WB-EMS training group. The participant's randomisation assignment was blinded to the assessment staff. All participants were requested to maintain their dietary habits the same as before the study and, during the time of the study, not follow any kind of diet, except on case of disease and by prescription of his/her doctor. If this was the case, they were withdrawn from the study. Individuals assigned to the control group were also requested not to change their physical activity habits or to engage in any kind of physical training programme. Individuals in the exercise groups were instructed not to perform additional exercise as per their intervention programmes.

Training modalities

A detailed description of each training modality is provided elsewhere [12].

The PAR group performed a concurrent training (combining aerobic and resistance training) based on the

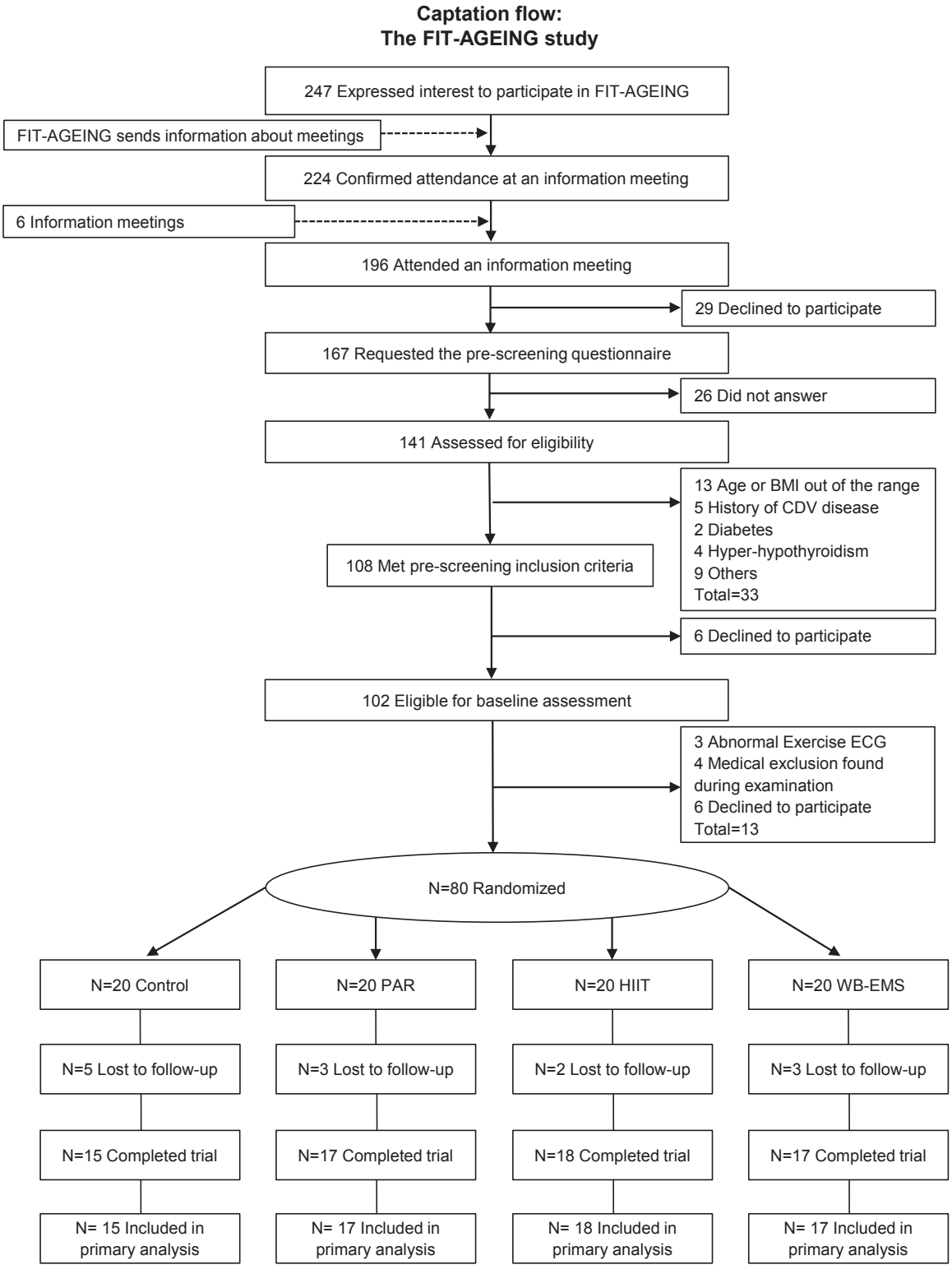

Figure 1 Flow-chart diagram. BMI, body mass index; CDV, cardiovascular; ECG, electrocardiogram; HIIT, high-intensity interval training group; PAR, physical activity recommendations for adults proposed by the World Health Organization group; WB-EMS, whole-body electromyostimulation group.

minimum physical activity recommended by the World Health Organization [15]. The participants trained 3 days week^{-1} for 12 weeks. The training volume was 150 min week^{-1} at 60–65% of the heart rate reserve for the aerobic training. The resistance training volume was approximately 60 min week^{-1} and the intensity was set at 40–50% of one-repetition maximum. The exercises programmed for the aerobic training section were treadmill, cycle-ergometer and elliptical ergometer. In addition, weight bearing and guided pneumatic machines were used in the resistance training section (i.e. squat, bench press, deadlift or lateral pull down). The participants performed compensatory exercises (core stability, flexibility and stabilisers muscles) aiming to minimise the risk of injuries, as well as to promote training adherence.

The HIIT group did an intervention programme was characterised by short and intermittent efforts of vigorous activity, interspersed with rest periods at passive or low-intensity exercises. The participants exercised 2 days week^{-1} for 12 weeks, performing two different complementary protocols [16]: (i) HIIT with long intervals (type A session) and (ii) HIIT with short intervals (type B session). The training volume was 40–65 min week^{-1} at >95% of the maximum oxygen uptake in the type A session and >120% of the maximum oxygen uptake in the type B session. The exercise chosen for type A session was treadmill with a personalised slope and the exercises programmed for the type B session were eight weight-bearing exercises in circuit form (i.e. squat, deadlift, high knees up, high heels up, push up, horizontal row, lateral plank and frontal plank).

The WB-EMS group performed a training programme that followed the same structure as that of the HIIT group (volume, intensity, training frequency, type of exercise and training sessions). However, we included electrical impulses to assess whether this training modality produced an extra effect. A bipolar symmetrical, and rectangular electric pulse was applied with: (i) a frequency of 15–20 Hz in the type A sessions and 35–75 Hz in the type B sessions; (ii) an intensity of 100 mA in the type A sessions and 80 mA in the type B sessions; (iii) an impulse breadth of 200–400 μs; and (iv) a duty cycle [ratio of on-time to the total cycle time: % duty cycle = 100/(total time/on-time)] of 99% in the type A sessions and 50–63% in the type B sessions. A WB-EMS device manufactured by Wiemspro (Malaga, Spain) was used.

All sessions started with a dynamic standardised warm-up, which included general mobility exercises and ended with a cooling-down protocol (active global stretching), which alternated five posterior chain exercises with five anterior chain exercises. A gradual progression was also proposed to control the exercise dose in each training group [12]. The starting level was individualised in each training group. All training modalities were delivered as planned.

A graduate in Sport Sciences provided general advice to the control group through an information meeting. They were instructed to maintain their lifestyle and not being enrolled in any training programme during the time of the study. The heart rate was monitored and the rated perceived exertion scale was registered during all sessions. Attendance at the training sessions was registered daily and participants were contacted upon any missing session to ask for the reason and motivate them to replace it on an alternative session. We registered an attendance of 99%, 98% and 99% of the supervised exercised sessions in the PAR, HIIT and WB-EMS groups, respectively from week 1 to week 12.

Dietary intake assessment

Dietary intake was assessed before (September) and after (December) the training programme (week 12) using the average of three 24-h recalls collected on nonconsecutive days (one weekend day included) by a trained research dietitian (LJ). This method is able to determine energy intake to within 8–10% of actual energy intake [17]. The interviews were meal-sequence based and involved a detailed assessment and description of the food consumed. Colored photographs of different portion sizes of foods were provided to help estimate the quantity of food consumed [18]. Dietary intakes from the 24-h recalls were analysed for calorie and macronutrient content using EVALFINUT software (https://www.finut.org/evalfinut), which is based on USDA (US Department of Agriculture) and BEDCA ('Base de Datos Española de Composición de Alimentos') databases.

Dietary energy density of foods and beverages (excluding drinking water) was calculated as total energy intake (kcal day^{-1}) divided by total weight of daily food intake (g day^{-1}) [19].

Food serving consumption was assessed using a food frequency questionnaire (FFQ) [20]. For each FFQ food item, a commonly used portion size was described (slices, cups, teaspoons, etc.) and the participants were asked how often they had consumed that unit on average over the last 3 months. Emphasis was added to ensure that the answers were related to long-term dietary factors and not to recent dietary changes. Each FFQ food item was converted into servings considering the standard portion weight of each FFQ food item collected in the own questionnaire (amount consumed/weight of portion).

Anthropometrics and body composition assessment

Anthropometric and body composition measurements were registered before and after the intervention programme (week 12), and the body mass index (BMI) calculated (weight/height^2). Weight and height were measured using an electronic scale (model 799; Electronic Column Scale, Hamburg, Germany). Lean mass and fat mass were evaluated by dual-energy X-ray absorptiometry (Discovery Wi; Hologic, Inc., Bedford, MA, USA) in accordance with the manufacturer's instructions. Lean mass index (LMI) and fat mass index (FMI) were calculated as lean mass/height^2 and fat mass/height^2, respectively.

Statistical analysis

The sample size and power calculations are made based on the data of a randomised control trial (The FIT-AGEING project [12]; clinicaltrial.gov: ID: NCT03334357). The principal aim of the FIT-AGEING study was to determine the effect of different training modalities on health-related parameters (i.e. body composition and sleep quality among others) in sedentary healthy adults. The determination of the sample size and power of the study were made based on the data of a pilot sample ($n = 30$). We considered different health-related parameters (i.e. body composition and sleep quality among others) differences between pre- and post-treatment in order to assess the sample size requirements for the one-way analysis of variance. As a result, we expected to detect a clinically relevant effect size of each variable (i.e. a loss of 3% of total body fat) considering a type I error of 0.05 with a statistical power of 0.85. To meet these criteria, a minimum of 14 participants per group was necessary. Assuming a maximum loss at follow-up of 25%, we decided to recruit 20 participants (approximately 50% women) for each study group. Therefore, in total, 80 participants (40 women and approximately 40 men) were enrolled in the FIT-AGEING study.

A Shapiro–Wilk test, visual check of histograms and Q-Q plots were used to verify the distribution of all variables. All data were normally distributed. The descriptive parameters are reported as the mean (SD).

Repeated-measures analysis of variance was used to determine changes in energy, fat, protein, carbohydrate and fibre intake, and dietary energy density across time, between groups, and its interaction (time × group). Student's *t*-tests for paired values were performed to evaluate differences in dependent variables before and after the intervention programme.

Analysis of covariance was used to examine the effect of groups (fixed factor) on dietary intake changes, namely post-energy intake minus pre-energy intake (dependent variable), adjusting for baseline values. The same analyses were performed for changes in fat, protein, carbohydrate and fibre intake, and dietary energy density.

All analyses were adjusted by sex, age, and sex and age. We performed Bonferroni *post hoc* tests with adjustment for multiple comparisons to determine differences between all exercise modality groups.

To examine the relationship between changes in dietary intake variables (energy, fat, protein, carbohydrate and dietary energy density) and changes in body composition variables (BMI, LMI and FMI), we conducted simple linear regressions. Multiple linear regressions were also performed to adjust by sex, age, and sex and age.

All analyses were conducted using SPSS, version 25.0 (IBM Corp. Armonk, NY, USA). $P < 0.05$ was considered statistically significant. Graphical presentations were prepared using PRISM, version 5 (GraphPad Software Inc., San Diego, CA, USA).

Results

Eighty middle-aged adults (40 women and 40 men) were enrolled in the study (Fig. 1). Table 1 shows the participant's baseline characteristics. Groups were similar in age, sex, BMI, LMI and FMI. Participants attended 98.7% of their exercise session and, in total, 13 participants withdrew between the randomisation and the follow-up. There were no adverse events occurring during the exercise sessions.

Figure 2 shows total energy intake (Fig. 2a), fat intake (Fig. 2b), protein intake (Fig. 2c), carbohydrate intake (Fig. 2d), fibre intake (Fig. 2e) and dietary energy density (Fig. 2f) before (September) and after (December) the intervention study. No time × group interaction was obtained in any dietary variable (all $P > 0.05$). When comparing within-group changes, the control group showed a slight but consistent higher energy intake in the final measurement (December) compared to baseline (September) [2291.1 (393.0) versus 2072.6 (419.6) kcal, $P = 0.036$, 95% confidence interval (CI) = 16.318 to 420.635 kcal]. All intervention groups and also the control group showed significantly lower protein intake after the intervention programme compared to baseline [76.6 (17.7) versus 53.5 (36.3) g, $P = 0.024$, 95% CI = −42.843 to −3.527 g for control group; 86.6 (22.3) versus 48.8 (32.6) g, $P = 0.003$, 95% CI = −60.798 to −14.710 g for PAR; 96.0 (40.8) versus 54.1 (42.6) g, $P = 0.006$, 95% CI = −70.045 to −13.695 g for HIIT; 90.2 (45.3) versus 49.4 (47.5) g, $P = 0.001$, 95% CI = −63.384 to −18.204 g for WB-EMS]. HIIT and WB-EMS groups showed significantly lower fibre intake after the intervention programme compared to baseline

Table 1 Descriptive parameters

	All (n = 67)	Control (n = 15)	PAR (n = 17)	HIIT (n = 18)	WB-EMS (n = 17)
Men (%)	47.8	40	47.1	50	52.9
Women (%)	52.2	60	52.9	50	47.1
Age (years)	53.3 (5.0)	51.7 (4.1)	54.9 (4.5)	53.1 (5.6)	53.4 (5.4)
Body mass index (kg m^{-2})	26.7 (3.8)	26.7 (3.9)	25.4 (2.9)	26.4 (3.1)	28.1 (4.7)
Lean mass index (kg m^{-2})	15.5 (2.8)	15.9 (3.1)	15.2 (2.5)	14.9 (2.9)	16.0 (2.9)
Fat mass index (kg m^{-2})	10.5 (2.9)	10.1 (2.7)	9.6 (2.7)	10.8 2.7)	11.3 (3.4)
Energy (kcal day^{-1})	2081.8 (485.4)	2072.6 (419.6)	2068.3 (392.1)	2205.9 (552.1)	1972.1 (556.6)
Fat (g day^{-1})	88.0 (25.0)	90.6 (23.4)	86.7 (18.5)	97.5 (30.6)	76.7 (22.6)
Protein (g day^{-1})	87.8 (34.1)	76.6 (17.7)	86.6 (22.3)	96.0 (40.8)	90.2 (45.3)
Carbohydrate (g day^{-1})	213.3 (64.8)	205.9 (45.4)	220.1 (65.5)	223.8 (71.0)	201.7 (74.2)
Fibre (g day^{-1})	28.4 (17.9)	28.0 (13.8)	28.5 (21.1)	28.4 (18.6)	28.4 (18.6)
Energy density (kcal g^{-1})	1.13 (0.21)	1.12 (0.17)	1.18 (0.19)	1.16 (0.21)	1.05 (0.26)

Data are shown as the mean (SD).
HIIT, high-intensity interval training group; PAR, physical activity recommendations for adults proposed by the World Health Organization group; WB-EMS, whole-body electromyostimulation group.

[28.4 (18.6) versus 14.4 (7.9) g, $P = 0.008$, 95% CI= −23.951 to −4.200 g for HIIT; 28.4 (18.6) versus 15.1 (9.1) g, $P = 0.023$, 95% CI = −24.537 to −2.108 g for WB-EMS]. We also found significantly higher dietary energy density in HIIT and WB-EMS after the intervention programme compared to baseline [1.17 (0.22) versus 1.27 (0.21) kcal g^{-1}, $P = 0.050$, 95% CI = 0.000 to 0.208 kcal g^{-1} for HIIT; 1.08 (0.25) versus 1.23 (0.23) kcal g^{-1}, $P = 0.028$, 95% CI = 0.020 to 0.296 kcal g^{-1} for WB-EMS]. No significant changes were found in the remaining variables. The same results were obtained when we expressed the macronutrient intake as the percentage of energy intake (see Supporting information, Figure S1).

Figure 3 shows changes in energy intake (Fig. 3a), fat intake (Fig. 3b), protein intake (Fig. 3c), carbohydrate intake (Fig. 3d), fibre intake (Fig. 3e) and dietary energy density (Fig. 3f) after the intervention study among the four groups. Fibre intake decreased in HIIT compared to the control group ($P = 0.041$; 95% CI = −25.660 to −0.319 kcal) and the results remained almost unchanged when we included sex and age as covariates (Table 2). The same results were obtained when we expressed the macronutrient intake as the percentage of energy intake (see Supporting information, Figure S1). Although without statistically significant intergroup differences, we observed tendencies in the lower energy intake in the training groups ($P = 0.079$) that become significant when we included sex, age and sex and age in the model (Table 2). Although no statistically significant intergroup differences were observed in the remaining variables, when we included sex and age in the model, energy intake, protein intake and dietary energy density become significant (Table 2).

A significant negative association was found between changes in energy intake and changes in LMI ($\beta = -0.001$, 95% CI = −0.001 to 0.000, $r^2 = 0.142$, $P = 0.002$) (Fig. 4a), which persisted after including sex, age, and both sex and age, in the model (all $P \leq 0.003$) (see Supporting information, Table S2). We observed a negative association between changes in fat intake and LMI ($\beta = -0.013$, 95% CI = −0.026 to −0.001, $r^2 = 0.067$, $P = 0.041$) (Fig. 4b), which persisted after including sex, age, and both sex and age, in the model (all $P \leq 0.042$) (see Supporting information, Table S2). We also found a negative association between changes in carbohydrate intake and LMI ($\beta = -0.004$, 95% CI = −0.007 to −0.001, $r^2 = 0.085$, $P = 0.021$) (Fig. 4d), which remained after including sex in the model ($P = 0.021$) (see Supporting information, Table S2) and disappeared when sex and sex and age were included as covariates (all $P > 0.05$) (see Supporting information, Table S2). No association was found between changes in protein intake and changes in LMI (Fig. 4c), as well as either changes in dietary energy density and changes in LMI (Fig. 4e) (all $P > 0.05$).

A significant positive association was found between changes in energy intake and changes in FMI ($\beta = 0.001$, 95% CI = 0.000 to 0.001, $r^2 = 0.095$, $P = 0.014$) (Fig. 4f), which remained after including sex, age, and both sex and age, in the model (all $P \leq 0.015$) (see Supporting information, Table S3). A significant positive association was also found between changes in fat intake and changes in FMI when we included age and both sex and age (all $P \leq 0.037$) (see Supporting information, Table S3) as covariates. No association was found between changes in protein and changes in FMI (Fig. 4h), changes in carbohydrate intake and FMI (Fig. 4i) and changes in dietary energy density and changes in FMI (Fig. 4j).

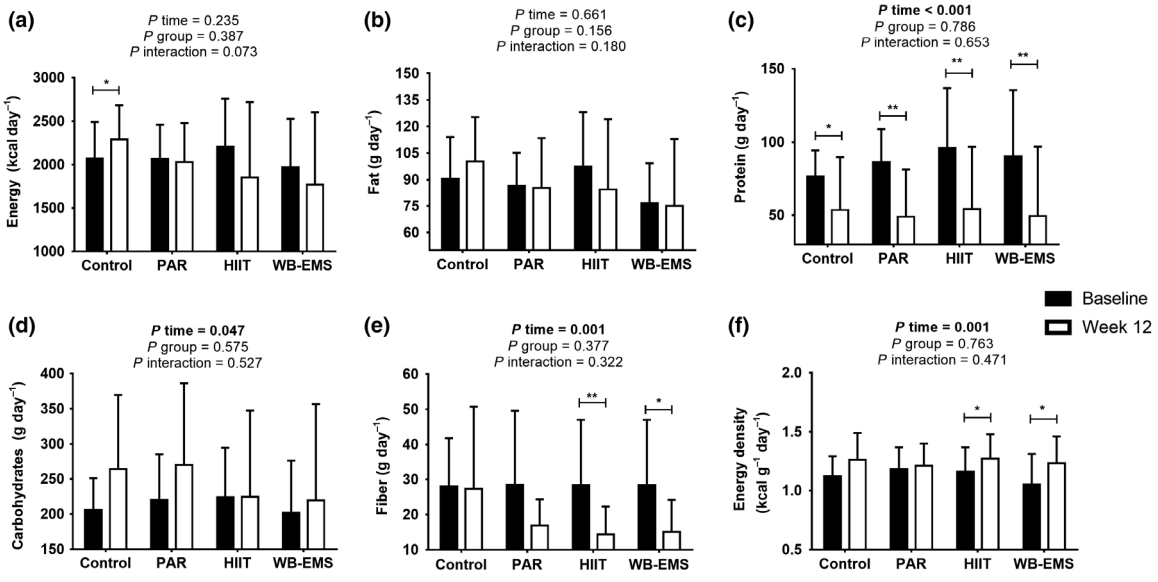

Figure 2 Dietary intake before and after the intervention study: energy (panel a), fat (panel b), protein (panel c), carbohydrate (panel d), fiber (panel e) and energy density (panel f). *P* value [time, group and interaction (time × group)] of repeated measures analysis of variance. $*P < 0.05$, $**P < 0.01$. Student's paired *t*-test. Data are shown as the mean (SD). HIIT, high-intensity interval training group; PAR, physical activity recommendations for adults proposed by the World Health Organization group; WB-EMS, whole-body electromyostimulation group.

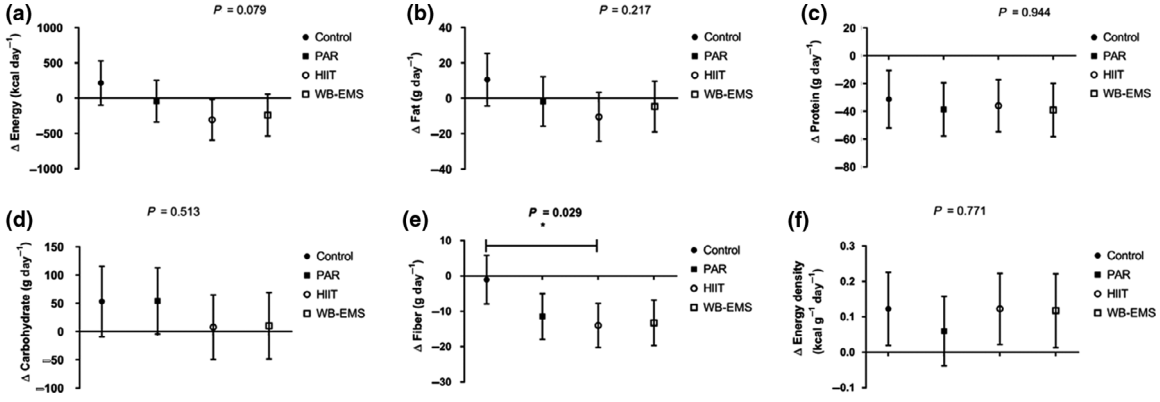

Figure 3 Changes in dietary variables after the intervention study among the four groups: energy (panel a), fat (panel b), protein (panel c), carbohydrate (panel d), fiber (panel e) and energy density (panel f). $*P < 0.05$, analysis of covariance adjusting for baseline values, with *post hoc* Bonferroni-corrected *t*-test. Data are shown as the mean (95% confidence interval). HIIT, high-intensity interval training group; PAR, physical activity recommendations for adults proposed by the World Health Organization group; WB-EMS, whole-body electromyostimulation group.

No associations were found between changes in any other dietary intake variables and changes in body composition variables (Fig. 4 and Table S4).

Table 3 shows changes in food group consumption across the study. Control group decreased olive oil and fish consumption ($P \leq 0.043$) (Table 3). The PAR group decreased egg consumption ($P = 0.034$) (Table 3). The HIIT group decreased fruit consumption ($P = 0.042$) (Table 3). The HIIT and WB-EMS groups increased legume consumption ($P \leq 0.049$) (Table 3). All groups increased alcoholic drink consumption ($P \leq 0.003$) (Table 3). Table 4 shows changes in body composition outcomes across the study. And Table S6 shows changes in dietary outcomes across the study.

Discussion

The main findings of the present study were that: (i) all groups, independently of training or the type of training, reduced their protein intake between the months of September and December; (ii) individuals training HIIT or HIIT plus WB-EMS increased their dietary energy density and reduced their fibre intake with no change in total energy intake or other dietary variables; and (iii)

Table 2 Changes in dietary intake outcomes adjusted for sex, age, and sex and age

	F	*P*	η^2
Energy intake (kcal)			
Model 1	2.890	**0.021**	0.192
Model 2	3.365	**0.009**	0.216
Model 3	2.968	**0.013**	0.229
Fat intake (g)			
Model 1	2.778	0.131	0.127
Model 2	2.219	0.064	0.154
Model 3	1.882	0.099	0.158
Protein intake (g)			
Model 1	5.573	**<0.001**	0.314
Model 2	8.572	**<0.001**	0.413
Model 3	7.108	**<0.001**	0.415
Carbohydrate intake (g)			
Model 1	2.206	0.065	0.153
Model 2	2.428	**0.045**	0.166
Model 3	2.144	0.061	0.177
Fibre intake (g)			
Model 1	8.098	**<0.001**	0.399
Model 2	7.696	**<0.001**	0.387
Model 3	6.828	**<0.001**	0.406
Dietary energy density (kcal g^{-1})			
Model 1	7.216	**<0.001**	0.388
Model 2	5.867	**<0.001**	0.340
Model 3	6.067	**<0.001**	0.394

Model 1, baseline values and sex; Model 2, baseline values and age; Model 3, baseline values, sex and age. *P* values (<0.05) are in bold.

body composition changes were dependent on dietary intake changes.

Despite no significant pre-post intragroup differences being observed in total energy intake, the groups training HIIT or HIIT plus WB-EMS showed a near-significant trend towards lower energy intake after the intervention programme. Our results concurred with those reported in a systematic review showing that exercise did not result in a compensatory increase in energy intake [8]. The appetite compensatory food responses to exercise display a high interindividual variability [21]. Although, when exercise is continued, energy intake could track total energy expenditure [21]. A previous study had shown that energy intake was not up-regulated as a compensatory response to the energy expenditure produced by exercise because of an increase in post-prandial satiety signalling driven by changes in gut peptides as a result of exercise [21]. In this sense, exercise could suppress the release of hormone acylated ghrelin (orexigenic) and could also up-regulate the secretion of polypeptide YY, glucagon-like peptide-1 and pancreatic polypeptide (anorexigenics), inducing a simultaneous appetite suppression [22].

We observed a reduction of protein intake in all groups after the intervention programme, whereas fat and carbohydrate intake did not change. Our results could be partially explained by a seasonality effect because our baseline assessment was performed in September and the

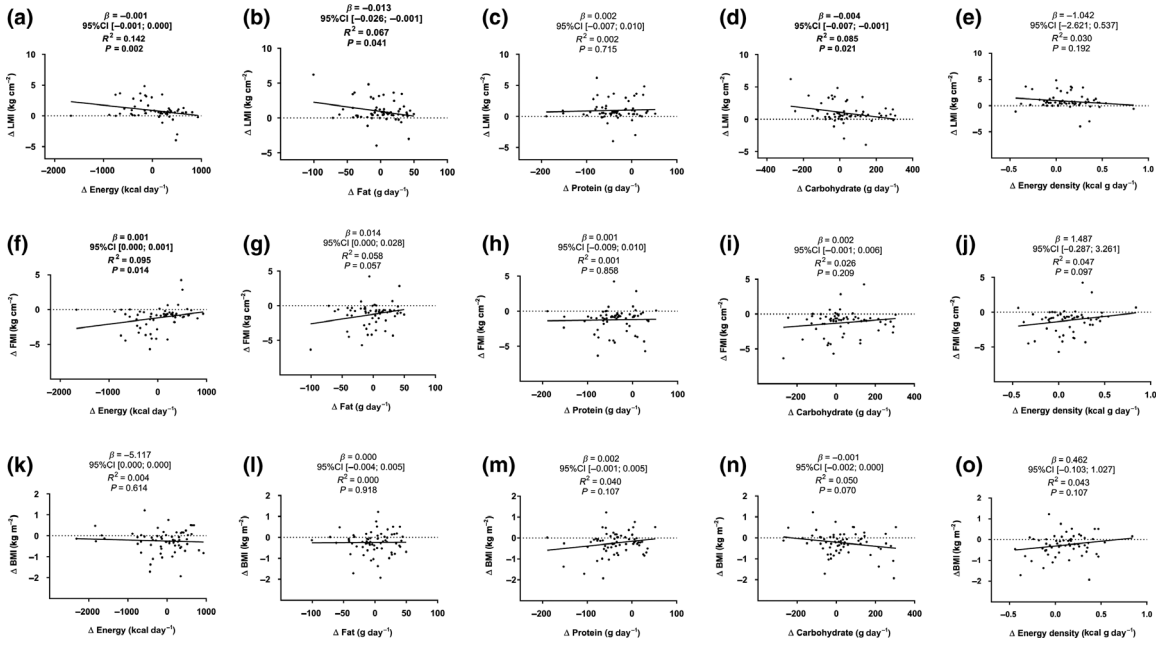

Figure 4 Association between changes in dietary variables: energy (a, f and k), fat (b, g and l), protein (c, h and m), carbohydrate (d, i and n), energy density (e, j and o), as well as changes in body composition variables: lean mass index (a, b, c, d and e), fat mass index (f, g, h, i and j) and body mass index (k, l, m, n, and o). β (unstandardised regression coefficient), r^2, and *P* from a simple linear regression analysis. BMI, body mass index; FMI, fat mass index; LMI, lean mass index.

Table 3 Changes in food group consumption

	Control			PAR			HIIT			WB-EMS		
	Δ	SD	*P*	Δ	SD	*P*	Δ	SD	*P*	Δ	SD	*P*
Dairy (servings day^{-1})	0.23	0.86	0.332	0.06	0.73	0.736	−0.01	0.89	0.956	−0.08	0.75	0.637
Vegetables (servings day^{-1})	−0.55	1.04	0.068	0.41	1.36	0.242	0.20	1.63	0.609	0.16	1.88	0.721
Fruits (servings day^{-1})	−0.60	1.20	0.082	−0.21	1.75	0.625	−0.60	1.16	**0.042**	−0.57	2.33	0.305
Cereals (servings day^{-1})	−0.01	1.71	0.977	0.04	1.62	0.922	−0.19	1.20	0.513	−0.38	1.10	0.146
Olive oil (servings day^{-1})	−0.54	0.89	**0.042**	−0.12	0.49	0.332	−0.11	0.83	0.579	−0.24	0.71	0.152
Eggs (servings week^{-1})	−0.07	1.60	0.870	−0.83	1.47	**0.034**	−0.31	0.83	0.133	−0.13	1.22	0.638
White meat (servings week^{-1})	−0.33	1.63	0.467	0.30	1.24	0.330	0.09	1.34	0.782	−0.18	1.24	0.531
Read meat (servings week^{-1})	−0.40	1.08	0.193	−0.29	0.88	0.189	−0.66	1.48	0.075	−0.35	1.45	0.311
Processed meat (servings week^{-1})	−0.09	4.40	0.938	0.36	3.00	0.634	−0.45	2.50	0.455	0.04	2.35	0.939
Fish (servings week^{-1})	−1.29	2.05	**0.043**	−0.32	2.25	0.566	−0.17	3.22	0.827	−0.55	2.81	0.401
Legumes (servings week^{-1})	0.32	1.46	0.421	0.45	1.03	0.093	0.64	1.29	**0.049**	1.06	1.81	**0.020**
Nuts (servings week^{-1})	−0.57	3.47	0.552	−0.54	3.98	0.586	0.06	3.86	0.946	−1.03	3.66	0.251
Vegetable oils (servings week^{-1})	0.03	1.12	0.913	0.03	0.64	0.863	0.00	0.16	1.000	−0.19	1.17	0.481
Margarine (servings week^{-1})	−0.18	0.57	0.268	−0.09	1.70	0.837	−0.22	2.43	0.708	−0.19	1.34	0.548
Butter (servings week^{-1})	0.50	1.98	0.367	0.00	0.63	1.000	−0.14	1.96	0.770	0.06	0.90	0.782
Sweets (servings week^{-1})	0.75	5.27	0.605	−0.71	7.52	0.701	3.64	7.69	0.061	1.34	3.57	0.119
Alcoholic drinks (servings week^{-1})	3.67	2.45	**<0.001**	4.81	5.64	**0.003**	5.33	3.94	**0.000**	6.88	8.68	**0.003**
Soft drinks (servings week^{-1})	0.07	1.33	0.849	0.51	2.68	0.443	−0.47	1.08	0.083	−1.26	2.81	0.066

Data are presented as mean of changes (Post minus Pre) and the SD. *P* value obtained from Student's paired *t*-test. *P* values (<0.05) are in bold.
HIIT, high-intensity interval training group; PAR, physical activity recommendations for adults proposed by the World Health Organization group; WB-EMS, whole-body electromyostimulation group.

Table 4 Changes in body composition outcomes

	Control			PAR			HIIT			WB-EMS		
	Δ	SD	*P*	Δ	SD	*P*	Δ	SD	*P*	Δ	SD	*P*
BMI (kg m^{-2})	−0.18	0.34	0.077	−0.51	0.66	**0.005**	−0.06	0.53	0.648	−0.23	0.44	**0.045**
LMI (kg m^{-2})	−0.10	1.67	0.818	0.80	1.10	**0.011**	1.27	1.33	**0.002**	1.71	1.67	**0.001**
FMI (kg m^{-2})	−0.07	1.82	0.892	−1.31	1.31	**0.001**	−1.51	1.67	**0.003**	−1.89	1.72	**<0.001**

Data are presented as the mean of changes (Post minus Pre) and the SD. *P* value obtained from Student's paired *t*-test. *P* values (<0.05) are in bold.
HIIT, high-intensity interval training group; PAR, physical activity recommendations for adults proposed by the World Health Organization group; WB-EMS, whole-body electromyostimulation group.

post-intervention assessment was conducted in December. In this sense, a systematic review and meta-analysis evaluated the effect of season on food intake in adults [23]. A higher consumption of eggs, meat and fish (high protein sources) was observed during spring–summer time [23] that concurred with our findings. Although without significant differences, we observed that all groups decreased the consumption of high protein sources (eggs, meat and fish), which could be clinically relevant to decrease the total intake of protein. When we computed a variable that includes all high protein sources (eggs, meat and fish), we found that all groups decreased their consumption of high protein sources [Control group, −3.3 (4.5) servings week^{-1}, $P = 0.001$; PAR, −0.4 (4.8) servings week^{-1}, $P = 0.007$; HIIT, −1.5 (4.4) servings week^{-1}, $P = 0.004$; WB-EMS, −1.2 (5.5) servings week^{-1}, $P = 0.071$]. Food seasonality could therefore be a factor determining dietary behavior and have an impact on food and energy intake [23]. It has been reported that there is a drop-in serotonin levels during the winter [24]. Low serotonin levels have shown to increase the intake of sweet carbohydrate-rich foods but not protein rich foods [25]. In this sense, we observed that exercise training does not influence food seasonality, producing an influence on the dietary intake of our participants. However, we have to take into account that all dietary outcomes were obtained from questionnaires, and so we should assume the possible bias of under-reporting or over-reporting in terms of protein intake.

In addition, it is well-known that protein intake showed a negative association with energy density [26]

and so an increase in dietary energy density could have related with a decrease in protein intake in our study cohort. Moreover, our results partially agree with a previous study that showed a fat, protein and carbohydrate intake reduction in sedentary individuals after 8 months of two different training programmes (i.e. aerobic and concurrent training) [6]. However, a recent systematic review suggested that there is no consistent evidence regardomg the effects of chronic exercise on macronutrient intake, showing that individuals do not spontaneously alter their diets in response to exercise [8].

Our results showed, for the first time, that HIIT and WB-EMS increased the dietary energy density and decreased the fibre intake. Thus, groups involved in the high-intensity exercise training programme increased the consumption of foods high in calories and low in fibre (i.e. processed foods). It has recently been suggested that an acute exercise bout increases the reward value of food with a higher wanting and preference for high-fat sweet foods (with high dietary energy density and low fibre content) in some sedentary obese individuals [27]. However, there is a lack of studies investigating the chronic effects of exercise on food reward. A previous study found no differences in appetite and food rewards in obese sedentary individuals after a moderate intensity training program and after a high-intensity training programme, respectively [28]. Although without significant differences, we observed that the HIIT and WB-EMS groups increased the consumption of sweets servings, which are low in fibre and have a high dietary energy density. We also observed a decrease in the consumption of fruits and cereals (high in fibre and with low dietary energy density) and an increase in alcohol consumption (low in fibre and with a high dietary energy density) in the HIIT and WB-EMS groups. Although we did not find significant differences in the consumption of the abovementioned food groups, the food pattern ingested by participants could be clinically relevant in terms of modifying the fibre intake and dietary energy density.

When we compared changes in dietary intake variables between the different training programmes, we did not find significant changes. To the best of our knowledge, this is the first study to compare PAR versus HIIT versus WB-EMS. Previous studies have demonstrated that there were no differences in dietary intake when comparing HIIT with moderate intensity continuous training [29], or comparing aerobic training versus PAR [6]. These results are in accordance with our results, indicating that there are no differences in terms of dietary intake between different training programmes.

Moreover, our results support the notion that exercise training induces muscle protein synthesis, providing an anabolic signal to the skeletal muscle independently of energy and/or macronutrient intake [30–32]. Exercise training could stimulate muscle protein synthesis up to 48 h after an exercise bout, demonstrating the potential benefits of exercise in terms of protein synthesis through the anabolic signal to skeletal muscle [31]. Exercise training increases muscle protein synthesis, likely shifting energy towards lean mass maintenance at the same time as stimulating fat depletion, to allow for fuel availability to cope with an increased energy demand [30]. Exercise could restore the catabolic signalling of low energy or macronutrient intake, increasing the rates of myofibrillar protein synthesis [30]. In addition, it has been suggested that changes in body composition after a supervised exercise programme would be dependent on the biological characteristic of the individual (classified as *Responders* or *Non-responders*) [9,27]. It has been suggested that exercise training induces muscle protein synthesis.

Our study has some limitations. First, the participants were sedentary middle-aged adults (45–65 years old) and we do not know whether these results can be extended to younger or physically active populations. Second, we used self-report methods to assess dietary outcomes, with the possible under-reporting or over-reporting of different unhealthy and healthy foods, which makes an accurate evaluation of the dietary intake difficult. Third, only two surveys were used to assess dietary outcomes and, furthermore, dietary outcomes were not controlled during the intervention program. Finally, the duration of our initial supervised training phase does not provide information regarding whether changes persisted beyond 12 weeks.

Conclusions

In conclusion, the present study study showed a seasonal effect in protein intake and this effect is not changed by training modalities (even when intensive) in healthy sedentary middle-aged individuals. However, higher dietary energy density and lower fibre intake were observed in high-intensity exercises modalities (HIIT and WB-EMS). Our results also suggest that lean mass gains induced by exercise are independent of energy or protein intake.

Transparency declaration

The lead author affirms that this manuscript is an honest, accurate and transparent account of the study being reported. The reporting of this work is compliant with CONSORT guidelines. The lead author affirms that no important aspects of the study have been omitted and that any discrepancies from the study as planned have been explained.

Conflict of interests, source of funding and authorship

The authors declare that they have no conflicts of interest.
No funding declared.
MJC was responsible for the conceiving the study. LJ-F was responsible for data curation. LJ-F and FJA-G were responsible for formal analysis. LJ-F, FJA-G and AD-l-O were responsible for the study investigation. FJA-G was responsible for study methodology. MJC was responsible for project administration. MJC was responsible for study supervision. LJ-F was responsible for writing the original draft. FJA-G and MJC were responsible for review and editing. All authors critically reviewed the manuscript and approved the final version submitted for publication.

References

1. Wiklund P (2016) The role of physical activity and exercise in obesity and weight management: time for critical appraisal. *J Sport Health Sci* **5**, 151–154.
2. Hruby A & Hu FB (2016) The epidemiology of obesity: a big picture. *Pharmacoeconomics* **33**, 673–689.
3. Lagerros YT & Rössner S (2013) Obesity management: what brings success? *Therap Adv Gastroenterol* **6**, 77–88.
4. Paes ST, Marins JCB & Andreazzi AE (2015) Metabolic effects of exercise on childhood obesity: a current view. *Rev Paul Pediatr* **33**, 122–129.
5. Ard JD, Miller G & Kahan S (2016) Nutrition interventions for obesity. *Med Clin North Am* **100**, 1341–1356.
6. Whellan DJ, Ellis SJ, Kraus WE *et al.* (2013) Aerobic and resistance training effects on energy intake: the STRRIDE AT/RT study: exercise training effects on energy intake. *Med Sci Sports Exerc* **151**, 414–420.
7. Howe SM, Hand TM & Manore MM (2014) Exercise-trained men and women: role of exercise and diet on appetite and energy intake. *Nutrients* **6**, 4935–4960.
8. Donnelly JE, Herrmann SD, Lambourne K *et al.* (2014) Does increased exercise or physical activity alter ad-libitum daily energy intake or macronutrient composition in healthy adults? A systematic review *PLoS ONE* **9**, e83498.
9. King NA, Hopkins M, Caudwell P *et al.* (2008) Individual variability following 12 weeks of supervised exercise: identification and characterization of compensation for exercise-induced weight loss. *Int J Obes* **32**, 177–184.
10. Khammassi M, Ouerghi N, Hadj-taieb S *et al.* (2018) Impact of a 12-week high-intensity interval training without caloric restriction on body composition and lipid profile in sedentary healthy overweight/obese youth. *J Exerc Rehabil* **14**, 118–125.
11. Kemmler W, Teschler M, Weißenfels A *et al.* (2016) Effects of whole-body electromyostimulation versus high-intensity resistance exercise on body composition and strength: a randomized controlled study. *Evid Based Complement Alternat Med* **2016**, 9236809.
12. Amaro-Gahete FJ, De-la-O A, Jurado-Fasoli L *et al.* (2018) Exercise training as S-Klotho protein stimulator in sedentary healthy adults: rationale, design, and methodology. *Contemp Clin Trials Commun* **11**, 10–19.
13. Schulz KF, Altman DG, Moher D *et al.* (2010) CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. *BMC Med* **8**, 18.
14. Schulz K & Grimes D (2002) Generation of allocation sequences in randomised trials: chance, not choice. *Lancet* **359**, 515–519.
15. WHO (2010) *Global Recommendations on Physical Activity for Health*. Geneva: World Health Organization Publications.
16. Buchheit M & Laursen PB (2013) High-intensity interval training, solutions to the programming puzzle: part I: cardiopulmonary emphasis. *Sports Med* **43**, 313–338.
17. Baugh E, Hedrick VE, Marinik EL *et al.* (2015) Dietary intake modification in response to participation in a resistance training program for sedentary older adults with prediabetes: findings from the resist diabetes study. *Eat Behav* **15**, 379–382.
18. López, MDR & Martín-Lagos, RA (2010) Guía para estudios dietéticos: álbum fotográfico de alimentos. ISBN: 9788433851673
19. Ledikwe JH, Blanck HM, Khan LK *et al.* (2005) Dietary energy density determined by eight calculation methods in a nationally representative United States population. *J Nutr* **135**, 273–278.
20. Vioque J, Navarrete-Muñoz E-M, Gimenez-Monzó D *et al.* (2013) Reproducibility and validity of a food frequency questionnaire among pregnant women in a Mediterranean area. *Nutr J* **12**, 26.
21. Hopkins M, King NA & Blundell JE (2010) Acute and long-term effects of exercise on appetite control: is there any benefit for weight control? *Curr Opin Clin Nutr Metab Care* **13**, 635–640.
22. King NA, Horner K, Hills AP *et al.* (2012) Exercise appetite and weight management: understanding the compensatory responses in eating behaviour and how they contribute to variability in exercise-induced weight loss. *Br J Sports Med* **46**, 315–322.
23. Stelmach-Mardas M, Kleiser C, Uzhova I *et al.* (2016) Seasonality of food groups and total energy intake: a systematic review and meta-analysis. *Eur J Clin Nutr* **70**, 700–708.
24. Ma Y, Olendzki BC, Li W *et al.* (2006) Seasonal variation in food intake, physical activity, and body weight in a predominantly overweight population. *Eur J Clin Nutr* **60**, 519–528.

25. Verschoor E, Finlayson G, Blundell J *et al.* (2010) Effects of an acute α-lactalbumin manipulation on mood and food hedonics in high- and low-trait anxiety individuals. *Br J Nutr* **104**, 595–602.
26. Stubbs J, Ferres S & Horgan G (2000) Energy density of foods: effects on energy intake. *Crit Rev Food Sci Nutr* **40**, 481–515.
27. Finlayson G, Caudwell P, Gibbons C *et al.* (2011) Low fat loss response after medium-term supervised exercise in obese is associated with exercise-induced increase in food reward. *J Obes* **2011**, 615624.
28. Martins C, Aschehoug I, Ludviksen M *et al.* (2017) High-intensity interval training, appetite, and reward value of food in the obese. *Med Sci Sports Exerc* **49**, 1851–1858.
29. Taylor J, Keating SE, Holland DJ *et al.* (2018) The chronic effect of interval training on energy intake: a systematic review and meta-analysis. *J Obes* **2018**, 6903208.
30. Sardeli AV, Komatsu TR, Mori MA *et al.* (2018) Resistance training prevents muscle loss induced by caloric restriction in obese elderly individuals: a systematic review and meta-analysis. *Nutrients* **10**, 4–6.
31. Hector AJ, McGlory C, Damas F *et al.* (2018) Pronounced energy restriction with elevated protein intake results in no change in proteolysis and reductions in skeletal muscle protein synthesis that are mitigated by resistance exercise. *FASEB J* **32**, 265–275.
32. Areta JL, Burke LM, Camera DM *et al.* (2014) Reduced resting skeletal muscle protein synthesis is rescued by resistance exercise and protein ingestion following short-term energy deficit. *Am J Physiol Endocrinol Metab* **306**, E989–E997.

Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Figure S1. Dietary intake before and after the intervention study (A, B and C).

Table S1. CONSORT 2010 checklist of information to include when reporting a randomised trial.

Table S2. Association of dietary variables changes with lean mass index changes.

Table S3. Association of dietary variables changes with fat mass index changes.

Table S4. Association of dietary variables changes with body mass index changes.

Table S5. Changes in body composition outcomes adjusted for sex, age, and sex and age.

Table S6. Changes in dietary outcomes.

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CLINICAL PRACTICE

Nice to know: impact of NICE guidelines on ketogenic diet services nationwide

V. J. Whiteley[1,2] K. J. Martin-McGill,[3,4] J. H. Carroll,[5] H. Taylor,[6] N. E. Schoeler[7] & on behalf of The Ketogenic Dietitians Research Network (KDRN)

[1]Therapy and Dietetics, Royal Manchester Children's Hospital, Manchester, UK
[2]School of Health & Society, University of Salford, Greater Manchester, UK
[3]Clinical sciences and nutrition, Universtiy of Chester, Chester, UK
[4]Institute of Translational Medicine, University of Liverpool, Liverpool, UK
[5]Institute of Health and Community, School of Health Professions, University of Plymouth, Plymouth, UK
[6]Dietetics, Sheffield Children's Hospital, Sheffield, UK
[7]Clinical Neurosciences, UCL Great Ormond Street Institute of Child Health, London, UK

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Correspondence
V. J. Whiteley, Therapy and Dietetics, Royal Manchester Children's Hospital, Oxford Road, Manchester M13 9WL, UK.
Tel.: +44 161 701 7580
Fax: +44 161 701 5052
E-mail: victoria.whiteley@mft.nhs.uk

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Abstract

Background: In 2012, the National Institute for Health and Care Excellence (NICE) Clinical Guidelines for Epilepsies: Diagnosis and Management (CG137) included, for the first time, ketogenic diets (KDs) as a treatment option for drug-resistant paediatric epilepsy. The recommendation was made to refer children and young people with epilepsy whose seizures have not responded to appropriate anti-epileptic drugs to a tertiary paediatric epilepsy specialist for consideration of the use of KDs. We aimed to assess the impact of this change in guidance on the numbers of ketogenic centres and patients following KDs for epilepsy in the UK and Ireland.
Methods: An online survey was circulated to ketogenic dietitians from the UK and Ireland. The results were compared with similar surveys published in 2000 and 2010.
Results: The number of centres offering KDs for treatment of epilepsy has risen from 22 in 2000, to 28 in 2010, and to 39 in 2017 (77% overall increase). Seven of these centres accept adult referrals, in comparison to only two centres in 2010. Patient numbers have increased from 101 in 2000 to 754 in 2017. In total, 267 patients are waiting to commence KD at 31 centres.
Conclusions: Over the last 7 years, the number of patients treated with a KD for epilepsy in the UK and Ireland has increased by 647%, with a 77% increase in the number of centres offering KDs. Despite this rapid growth, there is ongoing demand for patients to be considered for dietary therapy, highlighting the need for continued expansion of KD services nationally.

Introduction

Ketogenic diets (KDs) are high-fat, restricted carbohydrate diets that have been used as a treatment for drug-resistant epilepsy from the 1920s onwards [(1)]. There are different types of KDs in use: the classical KD [(2)], medium chain triglyceride (MCT) KD [(3)], Modified Atkins diet (MAD) [(4)] modified ketogenic diet (MKD) [(5,6)] and the low glycaemic index treatment (LGIT) [(7)]. The MAD, MKD and LGIT are less restrictive versions of a KD, often using household measures rather than accurate weighing of foods, with a greater freedom in the consumption of protein and, in some cases, carbohydrate. This more liberal approach may help improve tolerability and adherence [(8)], although the principles of a high-fat, low-carbohydrate diet remain, requiring significant dietary adjustment for the child, young person or adult undertaking KD therapy.

KDs are a well-established non-pharmacological treatment for drug-resistant epilepsy, as indicated by an

increasing number of randomised controlled trials (RCTs) in the paediatric population. The most recent Cochrane review (2018) [8] concluded that evidence from 10 trials showed promising results for the use of KDs in epilepsy treatment. A seizure reduction ≥50% was achieved in 38–85% [9,10] of participants treated with classical 4:1 KD and 42–60% [11,12] of participants treated with MAD for a duration of 3 months. Seizure freedom varies, with 1–55% [9,10] of participants following a classical KD and 10–25% [11,12] following a MAD for 3 months achieving this.

KDs are being increasingly used for adults with epilepsy and both the classical KD and MAD show promise in terms of feasibility and tolerability [13–15]. Effectiveness was recently assessed in two RCTs comparing MAD to control (treatment as usual). Zare *et al.* [16] reported 35.3% of participants to be responders achieving >50% reduction in seizure frequency after 2-month treatment with MAD. By contrast, Kverneland *et al.* [17] found only 12.5% of participants experienced >50% seizure reduction after 3-month treatment with MAD. However, this finding was not statistically significant. At best, they report a significant reduction in diet versus control group for moderate benefit only (25–50% seizure reduction). Low participant numbers, epilepsy type (focal versus generalised) and length of time with drug-resistant epilepsy are possible reasons for difference in findings. Further, large scale RCTs are required in this area.

The use of KDs to treat childhood epilepsy in the UK was examined in 2000 [18] and then again in 2010 [19] via a survey to paediatric ketogenic dietitians. The number of centres offering KDs and patients following a KD increased in this time period. These surveys were undertaken prior to 2012 and the publication of the National Institute for Health and Care Excellence (NICE) guidance on the diagnosis and management of epilepsies (CG137; 2012) [20] which, for the first time, recommended consideration of a KD for children and young people with drug-resistant epilepsy. One may expect that referrals for KD therapy and demand on KD services would have increased further subsequent to the change in NICE guidance [20]. The present survey aimed to reassess the use of KDs aiming to assess the changes in practice and service provision since 2007.

Materials and methods

An online survey was devised by a group of adult and paediatric ketogenic dietitians, as part of the Ketogenic Dietitians Research Network (KDRN). The survey comprised 44 questions (see Appendix 1) including questions regarding the number of services offering KD therapy, number and age of patients treated, waiting time to commence KD, duration on KD, and types of KD in use. The survey was circulated via the KDRN and Ketogenic Professional Advisory Group (KetoPAG) mailing lists and advertised through the parental support charities, Matthew's Friends and The Daisy Garland. Each service was asked to complete only one survey. Data were collected in July 2017 and approved by the audit and research departments of individual centres as required. The results were compared with the findings of earlier surveys published in 2000 [18] and 2010 [19].

Results

Demographics

Twenty-five KD services across the UK and Ireland completed the full survey. An additional 14 KD services provided data on the number of patients being treated with KD and those waiting to commence treatment, although they declined or were unable to complete the full survey for unreported reasons.

Ketogenic diet services

The number of services offering KDs for the treatment of epilepsy grew from 22 in 2000, [18] to 28 in 2010 [19], and to 39 in 2017, representing a 77% increase (Fig. 1).

Figure 2 shows the 39 centres in the UK and Ireland offering a service in 2017, with comparative size and patient group (paediatric, adult or both) treated. Two services offered KD therapy to adults in 2010 [19] compared to seven in 2017.

Number of patients

The number of patients with epilepsy being treated with a KD increased from 101 in 2000 [18], to 152 in 2010 [19], and to 754 in 2017 (Fig. 3) over a seven-fold increase. Thirty-one services had a waiting list, with 276 patients in total (range 1–49) waiting to commence a KD.

Types of ketogenic diet used

Twenty-six (of 39) ketogenic services responded to this section of the survey. Furthermore, 324/580 (55.9%) patients were following a classical KD, 187/580 (32.2%) were following a MKD, 56/580 (9.7%) were following a MCT KD and 13/580 (2.2%) were following a LGIT (Fig. 4a). The classical and MCT KDs were the only diets in use in 2000 [18] and 2010 [19].

In 2017, of the 324 patients following a classical KD, 142 (43.8%) were orally fed, 36 (11.2%) were enterally and orally-fed, and 146 (45%) were fully enterally-fed. Of the 187 patients following MKD, 183 (97.9%) patients fed orally, three (1.6%) were both enterally and orally-fed, and

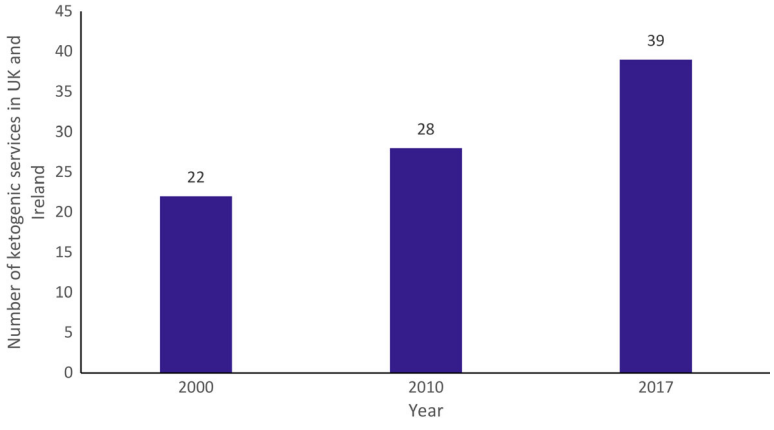

Figure 1 Number of ketogenic diet services per year [18,19].

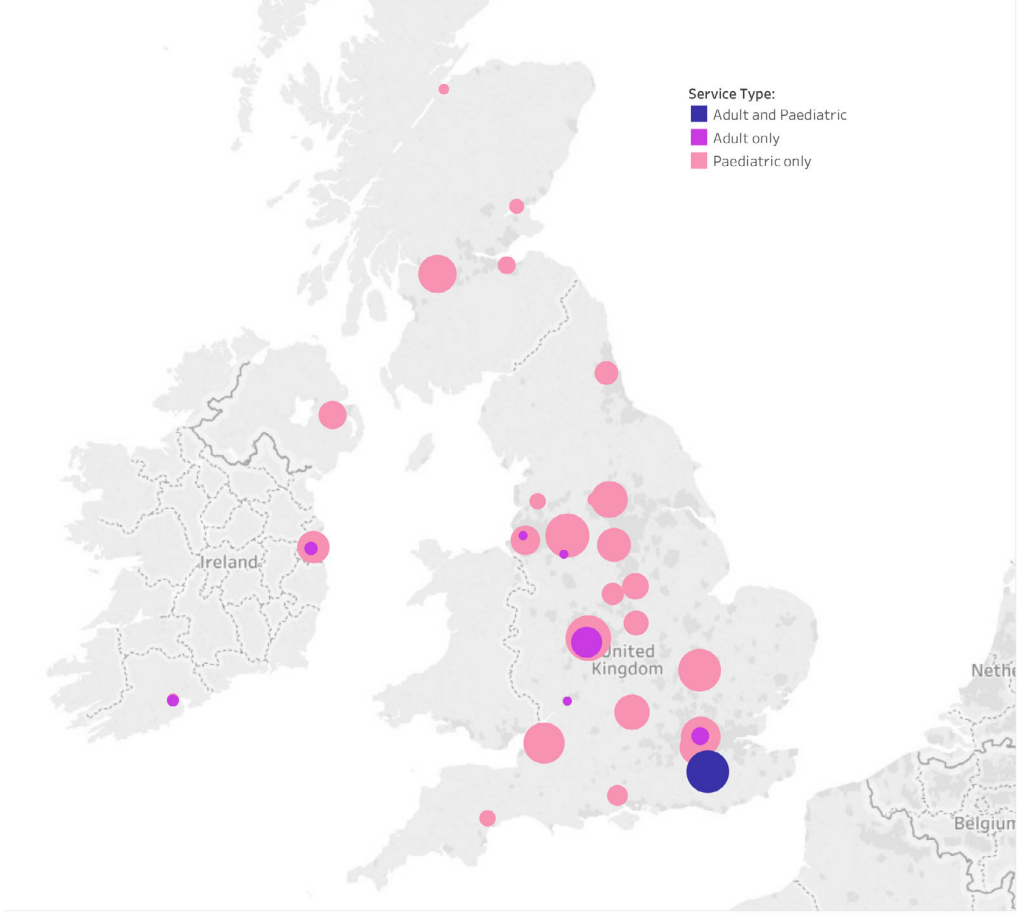

Figure 2 Map of ketogenic diet services in the UK and Ireland.

one (0.5%) was fully enterally-fed. Of the 56 patients following MCT KD, 40 (71.4%) fed orally, eight (14.2%) were enterally and orally-fed, and eight (14.2%) were fully enterally-fed. Thirteen (100%) patients were following a LGIT orally. No service reported use of the MAD (Fig. 4b).

Ketogenic diet initiation

In total, 180/580 (31%) of patients commenced a KD in the acute hospital setting which is similar to 43/132 (33%) of patients in 2010 [19] and 52/101 (51%) in 2000 [18]. The remainder commenced a KD at home as an outpatient.

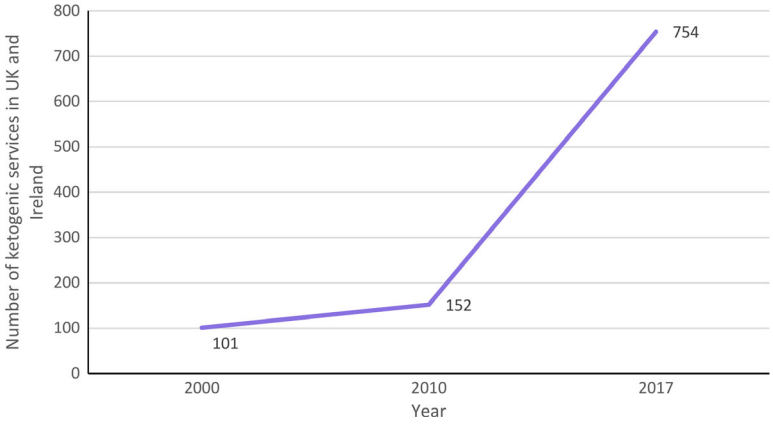

Figure 3 Number of patients on a ketogenic diet, 2000–2017 [18,19].

Figure 4 (a) Comparison of ketogenic diet (KD) types used over time. (b) Comparison of KD for orally fed children (%).
MCT, Medium chain triglyceride; MKD, Modified ketogenic diet; LGIT, Low glycaemic index treatment.

Ketogenic diet service provision

Seven of 26 (27%) of ketogenic services were supported by charity funding, with the remainder funded predominantly by the health service. Almost half of all ketogenic services reported inadequate funding for dietitians (11/26; 42%), with some centres reporting inadequate funding for nurses (3/26; 12%) and consultants (2/26; 8%), with limited service provision for new patients. Furthermore, 176/580 (30.3%) patients were treated with a KD for over 2 years and four services stated that this extended use of KD treatment limited their service provision for new patients. Only five services had access to a transition service for children ≥18 years; the shortage of transition services also limited ketogenic service provision.

Discussion

The number of KD services has increased by over two-thirds since 2000, with a concomitant increase of 647% in patient numbers. This is likely partly a result of the growing body of evidence supporting use of the KD for epilepsy [8] and the inclusion of KDs in NICE guidance

[18 1918,19]. A similar study of French KD services [21] also reports an increase in the number of KD services and patients treated from 2005 to 2018.

The use of the classical KD has reduced substantially since 2000, predominantly replaced by the MKD, which almost half of all orally-fed patients in this survey are following. Despite the lack of published evidence for the effectiveness of MKD for epilepsy, the use of this KD variant may have increased because it is viewed as easier to implement by dietitians, reducing the dietetic time required to calculate the dietary prescription and to educate patients [8]. The less restrictive MKD may be better tolerated and have higher compliance levels compared with the classical and MCT KDs, although further research is needed to support this and to determine its efficacy for epilepsy.

In 2000, it was common practice to initiate KD in the acute hospital setting [18] and the original International Consensus Statement (2009) [22] on Optimal Clinical Management of KDs in epilepsy supported this practice. In 2010 [19], half of all responding centres initiated KDs on an outpatient basis. This trend continued in our survey, with the majority of ketogenic services in the UK and Ireland favouring outpatient KD initiation. The patients who commenced KD in the acute setting may have been admitted for other reasons, including poor epilepsy control rather than exclusively to start a KD. Commencing a KD as an outpatient is generally less resource-intensive for the service and is likely to be less of a burden for families.

Although not yet recommended as part of current NICE guidance, there has been an increase in the availability of adult services. Research into KD use in this patient group is increasing [(16,17,23)], although studies are limited by small sample sizes and there remains a need for a large scale RCT exploring clinical and cost-effectiveness. Our survey has highlighted that one-third of patients on a KD remain on diet over the recommended 2-year treatment period [24], which could contribute to the greater demand for adult services. Disappointingly, despite the introduction of some adult services, only five of 26 (19%) of paediatric centres stated they had access to an adult or transition service to refer their older patients (≥18 years) to. This is an ongoing challenge for the managing paediatric ketogenic team but, more significantly, the family who may have to consider weaning their child from KD, even when a positive response is still maintained.

The present study has some limitations. The survey was not validated and could be subject to reporter bias. Although this was a practical and cost-efficient method of contacting nationwide ketogenic services, missing or incomplete data are inevitable, and the time restraints of clinical practice may have limited the depth of response on some occasions. On analysing the data, this provided more questions: how long patients are waiting to access KD services; why are patients staying on diet over 2 years; and what service adjustments or improvements are being implemented to reduce waiting lists or waiting times?

In conclusion, there is ongoing demand for KD for both paediatric and adult patients. Despite the rapid increase in services and increased availability of the diet, there are still substantial waiting lists, highlighting the need for continued expansion of services nationally. With almost 80% of services stating that the service size is limited by funding, new models of service delivery and funding need to be found to ensure that patients can access an effective treatment in a timely manner.

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Transparency declaration

The lead author affirms that this manuscript is an honest, accurate and transparent account of the study being reported. The lead author affirms that no important aspects of the study have been omitted and that any discrepancies from the study as planned have been explained.

Conflict of interests, source of funding and authorship

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KJM-M, VJW and NES contributed to the design and circulation of the study, the collation of data, and the initial analysis. VJW and HT contributed to the analysis and interpretation of the data. VJW and JHC contributed to the drafting of the manuscript. KJM-M and NES contributed to the review of the manuscript. The Ketogenic Dietitians Research Network (KDRN) is a consortium of ketogenic dietitians who collaborate on research projects to champion dietetic-led research and improve the evidence base for ketogenic dietetics in neuroscience. All authors critically reviewed the manuscript and approved the final version submitted for publication.

References

1. Wilder RM (1921) The effects of ketonemia on the course of epilepsy. *Mayo Clin Proceed* **2**, 2.
2. Neal EG, Chaffe H, Schwartz RH *et al.* (2008) The ketogenic diet for the treatment of childhood epilepsy: a randomised controlled trial. *Lancet Neurol* **7**, 500–506.
3. Huttenlocher PR, Wilbourn AJ & Signore JM (1971) Medium-chain triglycerides as a therapy for intractable childhood epilepsy. *Neurology* **21**, 1097–1103.
4. Kossoff EH, Cervenka MC, Henry BJ *et al.* (2013) A decade of the modified Atkins diet (2003–2013): results, insights, and future directions. *Epilepsy Behav* **29**, 437–442.
5. Martin-McGill KJ, Marson AG, Tudur Smith C *et al.* (2017) Ketogenic diets as an adjuvant therapy in glioblastoma (the KEATING trial): study protocol for a randomised pilot study. *Pilot Feasability Stud* **3**, 67.
6. Martin-McGill KJ, Lambert B, Whitelely VJ *et al.* (2019) Understanding the core principles of a 'modified ketogenic diet': a UK and Ireland perspective. *J Hum Nutr Diet* **32**, 385–390.
7. Pfeifer HH & Thiele EA (2005) Low-glycemic-index treatment: a liberalized ketogenic diet for treatment of intractable epilepsy. *Neurology* **65**, 1810–1812.
8. Martin-Mcgill KJ, Jackson CF, Breshnahan R *et al.* (2018) Ketogenic diet and other dietary treatments for epilepsy. *Cochrane Database Syst Rev*, Art. No.: CD001903.
9. Neal EG, Chaffe H, Schwartz RH *et al.* (2009) A randomized trial of classical and medium-chain triglyceride ketogenic diets in the treatment of childhood epilepsy. *Epilepsia* **50**, 1109–1117.
10. Seo JH, Lee YM, Lee JS *et al.* (2007) Efficacy and tolerability of the ketogenic diet according to lipid: nonlipid ratios-comparison of 3:1 with 4:1 diet. *Epilepsia* **48**, 801–805.
11. Kim JA, Yoon JR, Lee EJ *et al.* (2016) Efficacy of the classic ketogenic and the modified Atkins diets in refractory childhood epilepsy. *Epilepsia* **57**, 51–58.
12. Kossoff EH, Turner Z, Bluml RM *et al.* (2007) A randomized, crossover comparison of daily carbohydrate limits using the modified Atkins diet. *Epilepsy Behav* **10**, 432–436.
13. Martin-McGill KJ, Jenkinson MD, Tudur Smith C *et al.* (2017) The modified ketogenic diet for adults with refractory epilepsy: an evaluation of a set up service. *Seizure* **52**, 1–6.
14. Schoeler NE, Wood S, Aldridge V *et al.* (2014) Ketogenic dietary therapies for adults with epilepsy: feasibility and classification of response. *Epilepsy Behav* **37**, 77–81.
15. Nei M, Ngo L, Sirven JI *et al.* (2014) Ketogenic diet in adolescents and adults with epilepsy. *Seizure* **23**, 439–442.
16. Zare M, Okhovat AA, Esmaillzadeh A *et al.* (2017) Modified Atkins diet in adult with refractory epilepsy: a controlled randomized clinical trial. *Iran J Neurol* **16**, 72–77.
17. Kverneland M, Molteberg E, Iversen PO *et al.* (2018) Effect of modified Atkins diet in adults with drug-resistant focal epilepsy: a randomized clinical trial. *Epilepsia* **59**, 1567–1576.
18. Magrath G, MacDonald A & Whitehouse W (2000) Dietary practices and use of the ketogenic diet in the UK. *Seizure* **9**, 128–130.
19. Lord K & Magrath G (2010) Use of the ketogenic diet and dietary practices in the UK. *J Hum Nutr Diet* **23**, 126–132.
20. National Institute for Health and Care Excellence (NICE). Epilepsies: diagnosis and management CG137. 2012.
21. Dozieres-Puyravel B, Francois L, de Lucia S *et al.* (2018) Ketogenic diet therapies in France: state of the use in 2018. *Epilepsy Behav* **86**, 204–206.
22. Kossoff EH, Zupec-Kania BA, Amark PE *et al.* (2009) Optimal clinical management of children receiving the ketogenic diet: recommendations of the International Ketogenic Diet Study Group. *Epilepsia* **50**, 304–317.
23. McDonald TJW & Cervenka MC (2018) Ketogenic diets for adult neurological disorders. *Neurtherapeutics* **15**, 1018–1031.
24. Kossoff EH, Zupec-Kania BA, Auvin S *et al.* (2018) Optimal clinical management of children receiving dietary therapies for epilepsy: updated recommendations of the International Ketogenic Diet Study Group. *Epilepsia Open* **3**, 175–192.

Appendix

1 What centre are you based at?
2 Please indicate whether your centre is: Primary, Secondary, Tertiary
3 What year did the ketogenic service start at your centre?
4 Is dietetic time funded as part of the ketogenic service?
5 Please indicate whether the service is for: Adults, paediatrics, inpatients, outpatients
6 What age of referrals do you accept? ≤12 months, 13–24 months, 25 months < 5 years, 5 < 11 years, 11 < 16 years, 16 < 19 years, 19 < 30 years, 30 < 40 years, 40 < 50 years, 50 < 60 years, 60 < 70 years, 70 < 80 years, 80+ years
7 How many patients do you currently have on your waiting list (from referral until seen by dietitian, including screening)?
8 How many patients are currently 'on diet' (testing ketones)?
9 In the past 12 months (1 July 2016 to 30 June 2017), how many patients have been referred to your service in total?

a In the past 12 months (1 July 2016 to 30 June 2017), how many patients have been referred to your service aged 12 months or under (age at referral)?
b In the past 12 months (1 July 2016 to 30 June 2017), how many patients have been referred to your service aged 13–24 months (age at referral)?
c In the past 12 months (1 July 2016 to 30 June 2017), how many patients have been referred to your service aged 25 months to <5 years (age at referral)?
d In the past 12 months (1 July 2016 to 30 June 2017), how many patients have been referred to your service aged 5 to <11 years (age at referral)?
e In the past 12 months (1 July 2016 to 30 June 2017), how many patients have been referred to your service aged 11 to <16 years (age at referral)?
f In the past 12 months (1 July 2016 to 30 June 2017), how many patients have been referred to your service aged 16 to <19 years (age at referral)?
g In the past 12 months (1 July 2016 to 30 June 2017), how many patients have been referred to your service aged 19 to <30 years (age at referral)?
h In the past 12 months (1 July 2016 to 30 June 2017), how many patients have been referred to your service aged 30 to <40 years (age at referral)?
i In the past 12 months (1 July 2016 to 30 June 2017), how many patients have been referred to your service aged 40 to <50 years (age at referral)?
j In the past 12 months (1 July 2016 to 30 June 2017), how many patients have been referred to your service aged 50 to <60 years (age at referral)?
k In the past 12 months (1 July 2016 to 30 June 2017), how many patients have been referred to your service aged 60 to <70 years (age at referral)?
l In the past 12 months (1 July 2016 to 30 June 2017), how many patients have been referred to your service aged 70 < 80 years (age at referral)?

10 In the past 12 months (1 July 2016 to 30 June 2017) how many patients have started the diet (testing ketones)?
11 In the past 12 months (1 July 2016 to 30 June 2017), how many patients have you managed from other centres (taken over care from other ketogenic centres)?
12 In the past 12 months (1 July 2016 to 30 June 2017), how many patients have discontinued the diet?
13 In the past 12 months (1 July 2016–30 June 2017), what has been the minimum number of patients on your waiting list (from referral until seen by dietitian, including screening)?

a In the past 12 months (1 July 2016 to 30 June 2017), what has been the maximum number of patients on your waiting list (from referral until seen by dietitian, including screening)?

14 In the past 12 months (1 July 2016 to 30 June 2017), what has been the maximum number of patients on your waiting list (from referral until seen by dietitian, including screening)?

a In the past 12 months (1 July 2016 to 30 June 2017), what has been the maximum waiting time (days) between the initial appointment (seen by the dietitian/MDT) and dietary training?

15 For this question, please state the main reason for dietary discontinuation for each patient

a Of those patients who have discontinued the ketogenic diet in the past 12 months (1 July 2016 to 30 June 2017), how many discontinued because they reached the end of planned treatment?
b Of those patients who have discontinued the ketogenic diet in the past 12 months (1 July 2016 to 30 June 2017), how many discontinued due to non-response?
c Of those patients who have discontinued the ketogenic diet in the past 12 months (1 July 2016 to 30 June 2017), how many discontinued because their initial response to treatment was not maintained?
d Of those patients who have discontinued the ketogenic diet in the past 12 months (1 July 2016 to 30 June 2017), how many discontinued due to an inability to tolerate the diet?
e Of those patients who have discontinued the ketogenic diet in the past 12 months (1 July 2016 to 30 June 2017), how many discontinued due to patient inability to comply with the diet?

f Of those patients who have discontinued the ketogenic diet in the past 12 months (1 July 2016 to 30 June 2017), how many discontinued due to parent/guardian/carer inability to comply with the diet?

g Of those patients who have discontinued the ketogenic diet in the past 12 months (1 July 2016 to 30 June 2017), how many discontinued as the patient deceased?

h Of those patients who have discontinued the ketogenic diet in the past 12 months (1 July 2016 to 30 June 2017), how many discontinued due to another reason (please specify)?

16 Who is in your MDT (dedicated part of ketogenic team and within job plan, including vacant posts)?

17 Patient specialty accepted: GLUT1 deficiency syndrome, Metabolic: other (all except GLUT1), Neurology

18 Is your service funded to provide clinics off site, e.g. outreach?

19 Is your service funded to provide community support, e.g. home or school visits?

20 Is there a local transition service available?

21 Does your service provide a transition service?

22 Do you accept out-of-area patients?

23 Do you accept private ketogenic patients?

24 Is your service provision limited?

a If answered 'yes' to question 24a, what limits your service provision?

25 Do you have a fixed capacity?

a If answered 'yes' to question 24a, what limits your service provision?

26 What types of ketogenic diets does your service offer?

27 In your current caseload, how many patients do you manage on a classical ketogenic diet who are orally fed?

28 In your current caseload, how many patients do you manage on a classical ketogenic diet who are enterally fed?

29 In your current caseload, how many patients do you manage on a classical ketogenic diet who are both orally and enterally fed?

30 In your current caseload, how many patients do you manage on a medium chain triglyceride ketogenic diet who are orally fed?

31 In your current caseload, how many patients do you manage on a medium chain triglyceride ketogenic diet who are enterally fed?

32 In your current caseload, how many patients do you manage on a medium chain triglyceride ketogenic diet who are both orally and enterally fed?

33 In your current caseload, how many patients do you manage on a modified ketogenic diet who are orally fed?

34 In your current caseload, how many patients do you manage on a modified ketogenic diet who are enterally fed?

35 In your current caseload, how many patients do you manage on a modified ketogenic diet who are both orally and enterally fed?

36 In your current caseload, how many patients do you manage on a low glycaemic index who are orally fed?

37 In your current caseload, how many patients do you manage on a low glycaemic index who are both orally and enterally fed?

38 In your current caseload, how many patients were started as an inpatient?

39 In your current caseload, how many patients were started as an outpatient?

40 In your current caseload, how many patients were started in ICU?

41 In your current caseload, how many patients use blenderised diets (either wholly or partially) via feeding tube?

42 Do you offer group education sessions to initiate the diet?

43 In your current caseload, how many patients have been on the diet for > 2 years? (Do not include patients who are currently weaning off diet)

44 If you have any additional comments, please write in the box below

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CLINICAL PRACTICE

Dietitians' perspectives of the barriers and enablers to delivering patient-centred care

R. Levey[1] L. Ball,[1,2] W. Chaboyer[2,3] & I. Sladdin[1,2]

[1]School of Allied Health Sciences, Griffith University, Gold Coast, QLD, Australia
[2]Menzies Health Institute Queensland, Griffith University, Gold Coast, QLD, Australia
[3]School of Nursing and Midwifery, Griffith University, Gold Coast, QLD, Australia

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Correspondence
R. Levey, School of Allied Health Sciences, Griffith University, Gold Coast, QLD 4222 Australia.
Tel.: 011 61 414220538
E-mail: rebecca.levey@griffithuni.edu.au

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Abstract

Background: Patient-centred care (PCC) is widely recognised as being important with respect to the delivery of quality health care. However, limited research has explored PCC in the dietetic context. In particular, dietitians' views of the barriers and enablers to delivering a patient-centred approach have not been investigated. Therefore, the present study aimed to explore primary care dietitians' perspectives of the barriers and enablers to delivering PCC.
Methods: The present study was situated in a constructivist–interpretivist paradigm and used qualitative methods. Both convenience and snowball sampling were used to recruit Australian Accredited Practising Dietitians (APD) who were working in primary care. Individual semi-structured interviews explored dietitians' perspectives of the barriers and enablers to delivering PCC. Data were analysed thematically.
Results: Twelve APDs were interviewed between March and April 2018. Seven themes were discovered: (i) challenges in defining PCC; (ii) valuing PCC; (iii) enacting PCC; (iv) requiring additional education in PCC; (v) evaluating one's own practice; (vi) workplace pressures and constraints; and (vii) keeping up with expectations.
Conclusions: These findings suggest that: (i) the meaning of PCC in dietetics should be clarified to ensure it is being practiced consistently; (ii) undergraduate curricula require a greater emphasis on PCC so that dietitians graduate with the necessary knowledge and skills; (iii) there is a need for more professional development training to facilitate uptake of PCC in practice; and (iv) quantitative measurement of PCC using validated instruments is needed to evaluate PCC in the dietetic setting. Addressing some of these factors may assist dietitians to adopt these practices.

Introduction

Patient-centred care (PCC) is fundamental to the safety and quality of health care [(1)]. This approach, which has been advocated in various health professions for many years [(2)], aims to provide care that is respectful of, and responsive to, individual patients' needs and preferences, ensuring patients' values guide decision-making [(3)]. Patient-centred care does not merely focus on a disease or condition but rather on individual patients and their psychosocial, spiritual and emotional needs [(4)]. There are clear ethical and clinical justifications for PCC [(5)].

Patient-centred care has been associated with benefits for patients, such as improved clinical care, better disease management, increased patient engagement, reduced anxiety, improved quality of life, decreased mortality and higher functional status [(3,6–8)]. It has been associated with enhanced doctor and patient satisfaction, as well as increased safety and cost effectiveness, in addition to family and staff satisfaction [(3)]. Despite the associated benefits

and clear justifications, challenges still exist regarding implementing and sustaining patient-centred practices.

There are a number of potential barriers that impact on the delivery of PCC [9]. Barriers identified in other healthcare contexts include variation in the definition of PCC [9], time constraints reported by health professionals [9–11], attitudes of health professionals [5,9] and attitudes and/or practices stemming from the traditional biomedical model of care [10]. It is important to understand these barriers so that strategies can be developed to address them. Researchers have also identified a number of factors that facilitate the delivery of PCC, including training and education, measurement and evaluation tools, and supportive work environments for health professionals [9,12,13].

Patient-centred care is important to dietetic practice but has not been a focal point in dietetic research. Although researchers have explored this topic in more depth in the dietetic context recently [14], little has been reported about the potential challenges with delivering PCC from dietitians' perspectives [15]. Understanding the underlying factors that might influence dietitians' adoption of PCC is important; without a thorough understanding of the contextual barriers and enablers, strategies aimed at enhancing the care dietitians provide may be unrealistic and unsustainable. The present study aimed to explore the barriers and enablers to delivering PCC from the perspective of primary care dietitians.

Materials and methods

This was situated in a constructivist–interpretivist paradigm. In this paradigm, researchers seek to explore participants' subjective understanding of phenomena and this understanding is elicited through interactive dialogue between the researcher and participant [16]. This paradigm assumes that multiple realities and truths exist [16]. Both participants and researchers co-construct this reality. Consistent with this paradigm, qualitative methods were adopted, which enabled a comprehensive exploration of participants' perspectives and experiences [17,18]. The study was approved by the institution's Human Research Ethics Committee (Ref No: 2018/123). The consolidated criteria for reporting qualitative research (COREQ) helped to guide this work [19].

Study sample and recruitment

Participants were Australian Accredited Practising Dietitians (APDs) working in primary care (i.e. working in private practice and conducting one-on-one consultations with patients). Although it is important to investigate this topic further in the dietetic context in general, the present study focused on dietitians who were working in primary care. Dietitians work autonomously and rely on developing relationships with patients that continue over time. This is especially important within the primary care setting where chronic diseases are managed long term[20]. Participants were contacted via: (i) the Dietitian Connection weekly e-Newsletter; (ii) the Dietitians Unite 2018 seminar (March 2018); and (iii) dietetic specific social media sites. Both convenience and snowball sampling were used [21]. Convenience sampling was considered appropriate for the present study because it provided the greatest possible coverage and maximised participation [21]. Snowball sampling was also used to support convenience sampling. Sampling continued until data saturation was reached (i.e. no new insights were emerging) [22].

Data collection

A semi-structured interview guide was developed based on a review of the relevant literature [8,13]. The guide was piloted with five participants including both practising dietitians and academic researchers. Minor adaptations were made to the interview guide based on pilot feedback and consideration by the research team. Once the final interview guide was agreed on by the research team, data collection commenced. Example questions included: 'In your own words, could you please define your understanding of the term patient-centred care and what it means to you?', 'How important do you think it is for dietitians to deliver patient-centred care?', 'What do you believe helps you provide patient-centred care?' and 'When consulting clients, what makes it difficult to deliver PCC?'. Participants completed semi-structured telephone interviews, which ranged from 24 to 44 min, with an average interview time of 34 min. The same researcher (RL) conducted all of the interviews. Interviews were recorded using a digital Dictaphone and transcribed verbatim. Interviews were conducted until data saturation was reached.

Data analysis and rigour

Data were analysed using six phases of thematic analysis: (i) familiarising yourself with the data; (ii) generating initial codes; (iii) searching for themes; (iv) reviewing themes; (v) defining and naming themes; and (vi) producing the report [23,24]. Thematic analysis uses an iterative, systematic and repetitive process to explore how people feel, think or behave in a particular context relative to a specific research question [25,26]. Themes were then grouped into barriers and enablers [26].

Various approaches were employed to increase methodological rigour. Memos were used throughout data collection and analysis to document the researcher's thoughts

and biases, and direct quotes have been provided to demonstrate the researchers interpretation of the raw data [27]. These strategies helped to ensure dependability of the findings [27]. For the purpose of reflexivity, the researcher documented personal reflections, interests and values [27–29]. Contact summary sheets were completed after each interview to highlight salient ideas and topics that arose, summarise information from target questions, and suggest any remaining questions to consider [30]. Meetings were conducted with four members of the research team (RL, IS, LB, WC) during data collection and analysis, which consisted of reviewing and refining preliminary themes and excerpts from the transcripts to enhance trustworthiness [27,28]. Trustworthiness is a term used by qualitative researchers to reach agreement and check that themes were reflective of the data. Participant characteristics are summarised using the mean (SD).

Results

Participant demographics

Twelve APDs working in primary care participated in semi-structured telephone interviews between March and April 2018. Eleven participants were female with an age of 32 (6.8) years. Participants were from four Australian states and one territory, had 6 (5.2) years practising as an APD, as well as 3.7 (1.7) years working in private practice.

Thematic analysis

Seven themes were identified regarding dietitians' perspectives of the barriers and enablers to delivering PCC: (i) challenges in defining patient-centred care; (ii) valuing patient-centred care; (iii) enacting patient-centred care; (iv) requiring additional education in patient-centred care; (v) evaluating one's own practice; (vi) workplace pressures and constraints; and (vii) keeping up with expectations. Although themes are numbered from (i) to (vii), they do not indicate the relative importance or weight, they have simply been numbered for convenience.

Challenges in defining patient-centred care

The first theme related to the challenges with defining PCC. Although dietitians' comments suggested that they valued PCC, their descriptions and definitions of PCC varied. No definition was provided in the interview guide. Rather, future work should develop a definition suitable for dietetics. Some dietitians claimed that they had never heard of PCC and others considered that PCC was a 'vague' concept with the meaning requiring clarification. Dietitians described PCC as subjective, resulting in dietitians practising PCC differently. Most dietitians described PCC as care that places patients at the centre. Other descriptions included: empowering patients, treating patients as individuals, considering patient' views and treating patients with respect. Although dietitians' descriptions shared similarities, they still varied, suggesting that different dietitians had different understandings of PCC:

> 'I think it's a bit of a vague definition of terminology and probably has many different meanings for many different people' (P6)

Valuing patient-centred care

The second theme illustrated that dietitians valued PCC. The dietitians' comments suggested that they viewed PCC as important in understanding patients and making patients' feel empowered, valued and supported. Most dietitians commented that they were motivated to deliver PCC and suggested that it was their natural tendency to be empathetic. They described PCC as being critical in facilitating patients to develop personal goals, thereby allowing patients' priorities to be addressed. Dietitians agreed that, when PCC was not adopted, patients left the consultation lacking clarity and were consequently less likely to adopt care plans:

> 'If patients don't feel empowered, a lot of the delivery of information can fall on deaf ears and may not actually be implemented or practiced' (P6)

Enacting patient-centred care

The third theme is closely related to the second theme 'challenges in defining PCC' because it described what dietitians considered PCC looked like in their practice. Some dietitians described enacting PCC as allowing the patient to drive the consultation, with the dietitian's job being to merely guide and assist the patient to find the answers themselves. Dietitians perceived that delivering aspects of PCC, such as communication and shared decision-making, enabled patients to feel independent, and that it was the dietitian's role to guide, rather than adopt an expert-driven approach. Importantly, dietitians also perceived that, apart from some professional development courses, there was insufficient support for providing PCC. Although some dietitians described enacting PCC, others considered that not all patients desired a patient-centred approach. Dietitians' comments suggested that different patients' attitudes, personalities and expectations influenced dietitians' approach to care. Dietitians perceived that patients' age, personality, level of understanding and

stage of behaviour change influenced their preferences for different approaches to care.

> 'I like to see the client as having the answers within themselves and I'm just the vector or the cheerleader to help them find the right path for them' (P5)

> 'I think they are more willing to make changes because it has been tailored to them as opposed to a generic approach which hasn't been tailored or doesn't meet their exact needs' (P1)

Requiring additional education in patient-centred care

The fourth theme related to dietitians' perceptions that PCC education was insufficient in the dietetic profession. Dietitians considered that undergraduate education did not provide the knowledge necessary to deliver PCC, describing a gap in their skills that reduced their confidence and competence with respect to delivering PCC:

> 'So [PCC] was something I felt was a real gap in my skills when I finished university and I initially didn't feel competent to work in private practice and I felt that was something I needed to address before I went into private practice' (P7)

Dietitians commented that a greater availability of resources and courses to offer practical advice and strategies relating to PCC was needed. They also thought that experience was essential in obtaining PCC skills and helped with time-management.

Evaluating one's own practice

Dietitians highlighted the importance of practice evaluation tools that both allowed dietitians to self-evaluate their practice, and patients to evaluate the care they received. Some dietitians perceived that self-evaluation was lacking in practice. Others described being unsure how to evaluate PCC and were not aware of any tools specifically designed to evaluate PCC. Dietitians discussed the importance of receiving feedback from patients because they found it difficult to know if patients were being honest with their feedback, or merely being polite:

> '... Somehow get feedback from patients, because like you can't really tell yourself in the consult, and the patient is being nice to you' (P3)

Lifelong mentoring was also considered crucial for debriefing and external validation, allowing dietitians to know if they were practising PCC effectively whilst also learning PCC skills from their mentors.

Workplace pressures and constraints

Dietitians described factors in the workplace that hindered their ability to deliver PCC. Dietitians' explained that it was challenging to provide enough information, explore and understand the patient's needs and preferences, as well as build a rapport with patients in the allocated time. Participants expressed conflicting views regarding their approach to addressing the issue of time. Although some dietitians described compromising, or 'sacrificing the quality' (P7) of care for the sake of time-management, others explained that they compromised their time-management by taking more time in consultations than was allocated to ensure patients received the right care. Time was described as a key barrier by almost all participants; some believed it would be less of a barrier if adequate training was provided. Additionally, in the private practice setting where patients are paying for consultations, the cost of appointments was also seen as a prohibitive factor, limiting patients' ability and/or desire to attend follow-up consultations:

> 'So I guess the cost of an appointment is prohibitive for many clients, I know many of my clients would see me far more regularly if finances were not an issue' (P7)

Keeping up with expectations

Theme seven highlighted that dietitians found it difficult to practice PCC when trying to keep up with the expectations from general practitioners and other allied health professionals involved in the patient's care. Some participants perceived that health professionals who wanted particular outcomes may not have been willing to work at the patient's pace. Dietitians also recognised expectations they placed on themselves, in terms of adhering to best practice guidelines regarding expectations of what to cover in initial consultations. Furthermore, dietitians described a tendency to rush and fix everything, as well as to accomplish everything in the first consultation to keep up with what they perceived were patients' expectations, consequently neglecting to spend time building rapport.

> 'Maybe GP expectations if it has been a referral, that you cover everything straight away as opposed to taking the time to build rapport and taking the time to do more open-ended questions and help the patient to discover some of the answers themselves' (P4)

> 'So, I think because I'm a helper and most dietitians have that in them that they just want to help people

and our tendency to rush in and want to fix everything can actually not be helpful when it comes to patient-centred care' (P5)

These themes reflect a number of barriers and enablers to the delivery of PCC. The themes 'challenges in defining PCC', 'workplace pressures and constraints' and 'keeping up with expectations' were potential barriers. Additional education in PCC and ability to evaluate one's own practice were seen as potential enablers. Themes that reflected both barriers and enablers included: valuing PCC and enacting PCC. Enablers to valuing PCC consisted of dietitians' motivation to deliver such care; however, it could also be perceived as a barrier regarding the knowledge to practice gap, with dietitians' perceptions of valuing PCC not always aligning with how it was enacted. The theme enacting PCC was an enabler, with dietitians describing aspects of PCC they considered as essential when delivering it in practice. How and with whom dietitians chose to enact PCC was a potential barrier because some dietitians had the perception that not all patients desired a PCC approach.

Discussion

The present study offers novel findings in terms of being the first study to specifically explore Australian primary care dietitians' perspectives of the potential barriers and enablers to delivering PCC. Previous studies have explored this topic from the viewpoint of patients [4] and/or other healthcare professionals [9,10,31–34]. Although the findings from the present study share some similarities with studies from other healthcare contexts [9,10,32–34], they are also unique in that they describe distinct, context specific findings regarding potential factors that can facilitate or hinder the delivery of PCC by primary care dietitians.

Inconsistencies in how PCC is defined were considered as a barrier. Dietitians commented that PCC was a 'vague' concept, lacking a single clear definition, resulting in dietitians' practising PCC differently. Most described it as care with the patient at the centre, which does not reflect the multidimensional nature of this phenomenon. Dietitians' also highlighted that, without a clear definition, it was difficult to determine whether they were implementing PCC appropriately. This finding aligns with the existing literature that describes how varying definitions of PCC can make it difficult for professionals to know *what* it is, as well as *how* to implement it [13,36]. Overall, these findings reinforce that, although PCC is globally recognised as important, it is sometimes poorly understood in practice

The second theme illustrated that dietitians clearly valued PCC. This finding is consistent with views expressed by 11 private practice dietitians in an Australian qualitative study [35]. Dietitians described wanting to adapt their practice in an effort to best serve their clients [35] but expressed differing views regarding what the role of a dietitian was in a patient-centred approach. In another Canadian study on dietitians understanding of PCC approach to nutrition counselling, dietitians described it as the meeting of two experts, the dietitian and the patient, whereas others described only themselves as the expert [15]. Although dietitians may value PCC, there appears to be a knowledge-to-practice gap. Findings from an integrative review on PCC in dietetic practice suggested that, even though dietitians valued PCC, they did not always adopt a patient-centred approach [14]. There may be underlying factors that influence their practice, which highlights the importance of understanding dietitians' views of these barriers and enablers to delivering PCC [16].

Some dietitians in the present study considered that not all patients desired PCC and that dietitians' ability to enact PCC was influenced by patients' attitudes. Interestingly, these views were also expressed by participants in a qualitative study conducted in the USA involving 24 primary care dietitians [37]. Dietitians thought some clients viewed them as the 'food police', with some clients being apprehensive about seeing them [37]. How, and with whom dietitians chose to enact PCC can be seen as either an enabler or barrier to the delivery of PCC. Interestingly, it seemed some dietitians appeared to assume that PCC was only appropriate for certain patients, with only some desiring a patient-centred approach. This is reflective of a lack of understanding regarding the meaning of PCC; care would not be truly patient-centred if it looked the same for each individual patient. Importantly, PCC should be appropriate for every patient, although it may be enacted differently depending on the patient's preferences and values.

Dietitians' thought their education in PCC was insufficient. They identified a gap in their skills that resulted in reduced confidence and competence with respect to delivering PCC, with training not readily available unless they actively sought it. Similarly, a Swedish synthesis of seven studies highlighted that health professionals who had previous training in PCC were more confident with respect to its delivery, often involving clients in decision-making and goal setting by the use of different strategies and tools to suit individual patients [9]. It was concluded that the successful implementation of PCC was dependant on well trained professionals with a genuine knowledge of PCC [8]. Similarly, an integrative review published in 2017 highlighted that dietitians who received post-registration training in aspects of PCC, such as communication skills, expressed improved confidence in interviews, enhanced relationships with patients and an ability to

cope with challenging clients [14]. Interestingly, a UK study surveyed 20 nurses regarding challenges with delivering quality care [38]. Nurses responded with a desire to become more patient-centred and advocated for further training, which was perceived to help with developing skills such as addressing patients' anxieties, involving patients in care, communicating effectively and giving patients information [38]. Overall, the findings from the present and previous research suggest that additional training in PCC may enable health professionals, including dietitians, to feel confident with respect to delivering PCC.

Dietitians emphasised the importance of practice evaluation tools. Empirical evidence also suggests that evaluation tools are important with respect to determining whether certain approaches are working and allowing modifications to practice where necessary [13,33,39]. Although there are a number of instruments designed to measure aspects of PCC, few have been developed for use in the primary care setting, and existing instruments vary in scope and content [39]. In particular, the lack of PCC measurement instruments validated in the dietetic context has made it challenging for dietitians to evaluate their practice, specifically regarding PCC. Recently, a dietitian-reported inventory was developed and tested to measure PCC in primary care dietetic practice, and this instrument will enable dietitians to evaluate and improve their delivery of PCC [40].

Workplace pressures and constraints in the dietetic setting such as time and finances were limiting factors. Dietitians' voiced concerns of inadequate time during consultations. This was also expressed by dietitians in Australian [14] and Canadian [15] studies, where time was seen as a barrier in the implementation of PCC, with perceptions that certain aspects of PCC, such as shared decision-making, required more time [14]. Similarly, in a cross-sectional study conducted in the UK involving 1158 dietitians, lack of time was perceived as a key barrier to adopting patient-centred practices [11]. By contrast, a qualitative study on evidence-based leaflets in maternity care showed that involving patients in decision-making had no major effect on the length and time of a consultation [41]. The findings from previous studies also indicate that, if discussions occur at earlier stages of the consultation, this may allow concise discussion later and eventually save time [41]. This was aligned with the dietitians' comments that clear communication with patients at the start regarding what the consultation would entail could improve time management. Financial limitations were also considered as a prohibitive factor. These issues are long-standing and are complex to resolve. It is important that dietitians are well trained with respect to delivering PCC regardless of these constraints.

The expectations of general practitioners and other allied health professionals was also perceived as a barrier to delivering PCC. Dietitians felt pressure from physicians to address client concerns immediately rather than spend time building rapport. A qualitative study involving 16 semi-structured interviews with general practitoners in England found that physicians were more likely to prioritise the biomedical aspects rather than explore patients' perspectives [42]. Interestingly, a qualitative study investigating patients' experiences of dietetic consultations in the UK found that, although most patients preferred a patient-led approach, some strongly desired the traditional 'biomedical' practitioner-led style. It is important that dietitians explore patients' individual preferences and tailor care accordingly [43]. Dietitians in the present study also expressed pressure from other allied health involved in the client's care, wanting particular outcomes and not willing to work at the clients' pace.

Overall, the findings of the present study highlight a number of barriers and enablers to the delivery of PCC. Research has previously explored this phenomenon in other healthcare professions but not specifically from dietitians' perspectives. Therefore, the present study provides distinct, context specific findings regarding potential factors that can facilitate or hinder the delivery of PCC, which can inform future dietetic practice, research and education.

Strengths and limitations

There are both strengths and limitations to the present study. A strength of this study was the use of the maximum variation; we intended to draw participants from a variety of locations, different age groups, and with a range of years' experience. This form of purposive sampling helps to ensure a range and depth of understanding of the phenomenon is achieved [44]. Despite this, some demographic groups are underrepresented, with all but one participant being female and no participants in their first year of practice. Therefore these findings may not be reflective of how male and new graduate dietitians conceptualise and enact PCC. Further, this study only sampled Australian dietitians working in primary care, so findings may not be generalisable to other settings (e.g. costs may not be a barrier in a public hospital where patients are not required to pay for their consultation). Therefore, it would be beneficial for future research to further explore this topic in other contexts and among varying groups of dietitians.

Qualitative research does not aim to achieve generalisability but intends to generate rich and contextual findings, which can be achieved with samples considered small by quantitative researchers [45]. Semi-structured interviews

produced in-depth data relating to a phenomenon not yet explored from the perspective of dietitians, making this study novel and important. A number of approaches were adopted to enhance methodological rigour of this study, as identified in the methods section. Data analysis commenced from the beginning of data collection, thus researchers were able to identify when no new themes were arising. Although the sample size is small, it is comparable to other qualitative studies conducted in this context [5,43,46,47]. Previous empirical work suggests the basis for themes can emerge with about six interviews, with twelve interviews being sufficient for saturation [45], however seminal work published over 20 years ago by Sandelowski, an international leader in the field stressed the sample size must ultimately judge the quality of information collected against what use it is for [44].

Finally, although the interviews yielded rich descriptions, these reflected participants' perceptions and may not have represented how they actually practiced.

Conclusions

The present study offers novel findings in terms of being the first study to explore Australian primary care dietitians' views of the barriers and enablers to delivering PCC. These findings can inform future strategies in practice, education and research. Specifically, the findings suggested that undergraduate curricula might require more emphasis on PCC, so that students are prepared for practice. Furthermore, a greater availability of workshops and courses relevant to PCC beyond graduation might enhance dietitians' confidence in patient-centred practices, particularly for those who have left University some time ago. The findings highlighted that dietitians require additional tools, so they can evaluate their practice in terms of PCC, proposing the need for future research to further focus on developing and validating such instruments. Dietitians may also require more support to deliver the best possible care, and all members of the multidisciplinary team should be aware of and support the implementation of PCC. Finally, a conceptual defintion and the dimensions that comprise it should be made clear so that dietitians are practising PCC consistently.

Transparency declaration

The lead author affirms that this manuscript is an honest, accurate and transparent account of the study being reported. The reporting of this work is compliant with COREQ [19] guidelines. The lead author affirms that no important aspects of the study have been omitted and that any discrepancies from the study as planned have been explained.

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Conflict of interests, source of funding and authorship

The authors declare that they have no conflicts of interest.

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RL, IS, LB and WC contributed to the design of the qualitative study. RL conducted all interviews and transcribed the audio recordings. RL, IS, LB and WC contributed to data analysis, as well as the drafting of the paper. All authors approved the final version of the manuscript submitted for publication.

References

1. Australian Commission on Safety and Quality in Health Care 2012 National Safety and Quality Health Service Standards. Sydney: ACSQHC.
2. National Clinical Guideline Centre 2012 Patient experience in adult NHS services: improving the experience of care for people using adult NHS services. London: NCGC.
3. Austalian Commission on Safety and Qaulity in Healthcare 2010 Patient-centred care: improving qaulity and safety by focusing care on patients and consumers. Sydney: ACSQHC.
4. Reynolds A (2009) Patient-centered care. *Radiol Technol* **81**, 133–147.
5. Sladdin I, Chaboyer W & Ball L (2017) Patients' perceptions and experiences of patient-centred care in dietetic consultations. *J Hum Nutr Diet* **31**, 188–196.
6. Meterko M, Wright S, Lin H *et al.* (2010) Mortality among patients with acute myocardial infarction: the influences of patient-centered care and evidence-based medicine. *Health Serv Res* **45**, 1188–1204.
7. Flach SD, McCoy KD, Vaughn TE *et al.* (2004) Does patient-centered care improve provision of preventive services? *J Gen Intern Med* **19**, 1019–1026.
8. Jha AK, Orav EJ, Zheng J *et al.* (2008) Patients' perception of hospital care in the United States. *N Engl J Med* **359**, 1921–1931.
9. Moore L, Britten N, Lydahl D *et al.* (2017) Barriers and facilitators to the implementation of person-centred care

in different healthcare contexts. *Scand J Caring Sci* **31**, 662–673.
10. Robinson JH, Callister LC, Berry JA *et al.* (2008) Patient-centered care and adherence: definitions and applications to improve outcomes. *J Am Acad Nurse Pract* **20**, 600–607.
11. Whitehead K, Langley-Evans S, Tischler V *et al.* (2009) Communication skills for behaviour change in dietetic consultations. *J Hum Nutr Diet* **22**, 493–500.
12. International Alliance of Patients' Organizations. What is patient-centred healthcare 2007 December 2018. Available at: http://iapo.org.uk/sites/default/files/files/IAPO%20Patient-Centred%20Healthcare%20Review%202nd%20edition.pdf (accessed January 2018).
13. Pelzang R (2010) Time to learn: understanding patient-centred care. *Br J Nurs* **19**, 912–917.
14. Sladdin I, Ball L, Bull C *et al.* (2017) Patient-centred care to improve dietetic practice: an integrative review. *J Hum Nutr Diet* **30**, 453–470.
15. MacLellan D & Berenbaum S (2007) Canadian dietitians' understanding of the client-centered approach to nutrition counseling. *J Am Diet Assoc* **107**, 1414–1417.
16. Ponterotto JG (2005) Qualitative research in counseling psychology: a primer on research paradigms and philosophy of science. *J Couns Psychol* **52**, 126.
17. Taylor SJ, Bogdan R, DeVault M (2015) Qualitative methodology. In: *Introduction to Qualitative Research Methods: A Guidebook and Resource*. pp. 7–8 [Taylor S, Bogdan R, DeVault ML, editors]. New Jersey: John Wiley & Sons.
18. Swift J & Tischler V (2010) Qualitative research in nutrition and dietetics: getting started. *J Hum Nutr Diet* **23**, 559–566.
19. Tong A, Sainsbury P & Craig J (2007) Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *Int J Qual Health Care* **19**, 349–357.
20. Cant R & Ball L (2015) Decade of Medicare: the contribution of private practice dietitians to chronic disease management and diabetes group services. *Nutr Diet* **72**, 284–290.
21. Research Methodology (2017) Convenience sampling [Internet]. Available at: https://research-methodology.net/sampling-in-primary-data-collection/convenience-sampling (accessed April 2018).
22. Wiley Online Library (2017) Data saturation. Available at: https://onlinelibrary.wiley.com/doi/full/10.1002/9781118901731.iecrm0060 (accessed April 2018).
23. Braun V & Clarke V (2006) Using thematic analysis in psychology. *Qual Res Psychol* **3**, 77–101.
24. Clarke V & Braun V (2013) Teaching thematic analysis: overcoming challenges and developing strategies for effective learning. *Psychologist* **26**, 120–123.
25. Guest G, MacQueen KM, Namey EE (2011) Grounded theory. In: *Applied Thematic Analysis*. pp. 13–14 [Knight VHL, Koscielak K, Virding A, editors]. Los Angeles, CA: Sage.
26. Fade S & Swift J (2011) Qualitative research in nutrition and dietetics: data analysis issues. *J Hum Nutr Diet* **24**, 106–114.
27. Nowell LS, Norris JM, White DE *et al.* (2017) Thematic analysis: striving to meet the trustworthiness criteria. *Int J Qual Methods* **16**, 1609406917733847.
28. Pilnick A & Swift J (2011) Qualitative research in nutrition and dietetics: assessing quality. *J Hum Nutr Diet* **24**, 209–214.
29. Draper A & Swift JA (2011) Qualitative research in nutrition and dietetics: data collection issues. *J Hum Nutr Diet* **24**, 3–12.
30. Miles, MB, Huberman, AM (1994) Early steps in analysis. In: *Qualitative Data Analysis: An Expanded Sourcebook*. pp. 50–89 [Holland R, editor]. Los Angeles, CA: Sage.
31. Olsson LE, Jakobsson Ung E, Swedberg K *et al.* (2013) Efficacy of person-centred care as an intervention in controlled trials–a systematic review. *J Clin Nurs* **22**, 456–465.
32. Gillespie R, Florin D & Gillam S (2004) How is patient-centred care understood by the clinical, managerial and lay stakeholders responsible for promoting this agenda? *Health Expect* **7**, 142–148.
33. Shaller D (2007) *Patient-centered Care: What Does It Take?* New York, NY: Commonwealth Fund.
34. Berghout M, van Exel J, Leensvaart L *et al.* (2015) Healthcare professionals' views on patient-centered care in hospitals. *BMC Health Serv Res* **15**, 385.
35. Harper C & Maher J (2017) Investigating philosophies underpinning dietetic private practice. *Behav Sci* **7**, 11.
36. Scholl I, Zill JM, Härter M *et al.* (2014) An integrative model of patient-centeredness–a systematic review and concept analysis. *PLoS ONE* **9**, e107828.
37. Devine CM, Jastran M & Bisogni CA (2004) On the front line: practice satisfactions and challenges experienced by dietetics and nutrition professionals working in community settings in New York State. *J Am Diet Assoc* **104**, 787–792.
38. West E, Barron DN & Reeves R (2005) Overcoming the barriers to patient-centred care: time, tools and training. *J Clin Nurs* **14**, 435–443.
39. De Silva D (2014) Helping measure person-centred care: a review of evidence about commonly used approaches and tools used to help measure person-centred care. London: The Health Foundation.
40. Sladdin I, Gillespie B, Ball L *et al.* (2019) Development and psychometric testing of an inventory to measure patient-centred care in dietetic practice: dietitian version. *J Hum Nutr Diet* /doi.org/10.1111/jhn.12644.
41. Stapleton H, Kirkham M & Thomas G (2002) Qualitative study of evidence based leaflets in maternity care. *BMJ* **324**, 639.

42. Blakeman T, Macdonald W, Bower P *et al.* (2006) A qualitative study of GPs' attitudes to self-management of chronic disease. *Br J Gen Pract* **56**, 407–414.
43. Hancock RE, Bonner G, Hollingdale R *et al.* (2012) 'If you listen to me properly, I feel good': a qualitative examination of patient experiences of dietetic consultations. *J Hum Nutr Diet* **25**, 275–284.
44. Sandelowski M (1995) Sample size in qualitative research. *Res Nurs Health* **18**, 179–183.
45. Guest G, Bunce A & Johnson L (2006) How many interviews are enough? An experiment with data saturation and variability. *Field Methods* **18**, 59–82.
46. Ball L, Davmor R, Leveritt M *et al.* (2016) Understanding the nutrition care needs of patients newly diagnosed with type 2 diabetes: a need for open communication and patient-focussed consultations. *Aust J Prim Health* **22**, 416–422.
47. McMahon AT, Tay P, Tapsell L *et al.* (2016) Building bridges in dietary counselling: an exploratory study examining the usefulness of wellness and wellbeing concepts. *J Hum Nutr Diet* **29**, 75–85.

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INFLAMMATORY DISORDERS

Perceptions and psychosocial impact of food, nutrition, eating and drinking in people with inflammatory bowel disease: a qualitative investigation of food-related quality of life

W. Czuber-Dochan[1] M. Morgan,[2] L. D. Hughes,[3] M. C. E. Lomer,[1] J. O. Lindsay[4,5] & K. Whelan[1]

[1]Department of Nutritional Sciences, Faculty of Life Sciences and Medicine, King's College London, London, UK
[2]Institute of Pharmacological Sciences, King's College London, London, UK
[3]Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK
[4]Barts Health NHS Trust, The Royal London Hospital, London, UK
[5]Centre for Immunobiology, Blizard Institute, Barts and the London School of Medicine, Queen Mary University of London, London, UK

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inflammatory bowel disease, food, nutrition, quality of life, qualitative study.

Correspondence
Dr W. Czuber-Dochan, King's College London, Franklin Wilkins Building, 150 Stamford Street, London SE1 9NH, UK.
Tel.: +44(0) 207848 4552
E-mail: wladzia.czuber-dochan@kcl.ac.uk

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Abstract

Introduction: Extensive research has provided an important understanding of the impact of inflammatory bowel disease (IBD) on nutrient intake, requirements and metabolism. By contrast, there has been limited research examining the psychosocial aspects of food, eating and drinking in IBD. The present study aimed to address this unmet need.
Methods: Qualitative semi-structured interviews regarding the perceptions and psychosocial impact of food, eating and drinking were undertaken with 28 purposively selected people with IBD. Interviews were audio-recorded and transcribed verbatim. Colaizzi's framework was used to structure the data analysis.
Results: Five major themes were identified. IBD symptoms and both surgical and medical treatments were described as having a direct impact on eating and drinking, with participants also using different food-related strategies to control IBD symptoms. These included a process of experimentation to identify trigger foods, following a severely restricted and limited diet, eating small portions, and eating more frequently. However, their limited knowledge about if, and how, food affected their symptoms, often resulted in negative coping strategies that impacted on psychosocial functioning, including a lack of enjoyment of eating, being afraid to eat and finding social occasions stressful. Managing food and drinking also made food shopping and preparation more burdensome, creating problems with families, at work and for social life, as well as the need for careful preparation and advanced planning of activities.
Conclusions: Inflammatory bowel disease has a profound impact on psychosocial aspects of food and nutrition, which impacts on 'food-related quality of life' (FRQoL). Further research is required to identify interventions that will improve FRQoL in patients with IBD.

Introduction

The treatment of inflammatory bowel disease (IBD) concentrates primarily on gastrointestinal and extra-intestinal symptom management [(1)]. The chronic nature of the condition and the difficult-to-manage symptoms of IBD, such as diarrhoea, abdominal pain, fatigue and weight loss, may affect many aspects of an

individual's life and may significantly impact their quality of life [2,3].

Extensive research over the past two decades has led to an improved understanding of the impact of IBD on nutrient intake, requirements and metabolism [4–7]. Although these aspects are crucially important, there has been limited research related to the psychosocial aspects of food, nutrition, eating and drinking in IBD, including social, emotional and cultural aspects, despite people with IBD considering this to be an important area for research [8,9].

Apart from numerous biological roles, food fulfils a host of social and psychological needs, such as being a source of pleasure, a coping mechanism, and communicating an individual's belonging to particular social and cultural groups [10,11]. These important psychosocial roles may be dramatically altered in people with IBD, especially because it can affect people of all ages, gender and ethnicities, for whom food may have a wide variety of roles and meanings. For example, eating may be associated with symptoms, malnutrition can limit daily life and diet therapy is used in disease management. Eating and drinking are also central to many social interactions with family, friends and colleagues and thus IBD can inhibit some people from socialising [12–14]. Indeed, one survey reported that 82% of people with IBD experienced problems with food and nutrition, including issues with trigger foods and impaired social activities [8]. Despite attempts to emphasise normality and control in their lives, some people with IBD experience negative psychosocial impacts associated with food, impacting on their food enjoyment and self-identity [13].

Despite previous research findings indicating that food, nutrition and social interactions are of high importance to people with IBD [8] and that they would like issues around diet and lifestyle to be discussed during clinical consultations [15], they have limited access to dietetic services [16] and inadequate support and advice in relation to understanding the psychosocial aspects of food in IBD [17]. The existing empirical research into experiences of food and nutrition in people with IBD is limited to small questionnaire surveys. The published qualitative studies predominantly conflate the experiences of people with various gastrointestinal disorders [12–14], although an online interview study in IBD identified numerous challenges experienced by people with IBD in relation to food, nutrition, eating and drinking and their impact on their lives [18]. Further studies into the psychosocial impact that eating and drinking can have for people with IBD are warranted. The aim of the present study was to explore the perceptions and psychosocial impacts of food, nutrition, eating and drinking on the lives of people with IBD.

Methods

In-depth, semi-structured qualitative interviews were conducted with people with IBD to explore the perceptions and psychosocial impacts of food, nutrition, eating and drinking. The study selection criteria were a confirmed diagnosis of either Crohn's disease (CD) or ulcerative colitis (UC), age 16 years or older (with no upper age limit), able to eat some normal food, able to consent for themselves and the ability to speak English fluently. Participants were excluded if they were currently treated with exclusive enteral or parenteral nutrition and did not eat solid food. Additionally, being pregnant or breastfeeding and a diagnosis of an eating disorder or chronic illness (e.g. end-stage renal disease) that could affect the participant's ability to eat and drink normally were also exclusions.

Patients were recruited from outpatient clinics at two large London teaching hospitals. Specialist clinics for general gastroenterology and IBD clinics were targeted for recruitment. A purposive sampling strategy was used. Potential study participants were identified during scheduled outpatient appointments by a member of the clinical team.

The interviews were based on questions developed drawing on the previous literature, including previous research undertaken by the study team [8], and focused on the issues of food and symptoms, food and social interaction with friends and family, effect of food and eating on symptoms, effects of food, eating and drinking on life and nutritional status, and adaptations to managing these issues (Table 1). For the purpose of clarity, the questions were reviewed by the research team and tested with one participant.

All interviews were conducted face-to-face, either in a quiet room at the university ($n = 5$), hospital ($n = 8$) or at the participant's home ($n = 10$) or place of work ($n = 5$), according to their preference. Participants were encouraged to talk openly about issues that had the most relevance to them and responses clarified and probed as necessary. All interviews were audio-recorded and transcribed verbatim by a professional transcriber. After 20 interviews were conducted, the subsequent interviews did not identify any new issues related to the topic of the study, indicating that saturation had been achieved. A further eight participants were interviewed both to examine whether data saturation was achieved, and because the participants had already agreed to take part in the study.

Thematic analysis was undertaken based on Colaizzi's 7 step framework [19] (Table 2). NVIVO, version 11 (QSR International Pty Ltd, Doncaster, VIC, Australia) for qualitative data analysis was used to manage data. To improve rigour of the study, two experienced qualitative researchers were involved in the data analysis (WCD and MM).

Table 1 Topic guide for semi-structured interviews relating to food, nutrition, eating and drinking in inflammatory bowel disease (IBD)

Stage of the interview process and content of the interview	Examples of probes used during the interview
Introduction and opening questions	
Length of time since diagnosis	Could you describe when you were diagnosed with inflammatory bowel disease and how your symptoms are?
IBD symptoms and impact on diet	Can you tell me if having IBD and the symptoms have affected the way you eat and drink? How do you feel about that? Since being diagnosed with IBD, have you made changes to your diet?
Follow-up questions to progress the interview	
Symptoms and trigger foods	Have you found any foods or drinks trigger your IBD symptoms?
Eating habits and any modifications to eating and drinking	Do you think your diet affects your IBD, and if so how? What other factors affect your diet (e.g. cultural, likes/dislikes, trying new foods)? Have these been affected by being diagnosed with IBD? Do you avoid particular foods or drinks? What are the reasons for avoiding them? Do you follow a special diet?
Food, family and socialising	Has having IBD affected your social life and going out to eat with family and friends? How does your eating and drinking affect your daily life?
Dietary advice	Since being diagnosed with IBD, do you have problems controlling your weight? Have you been given any diet specific advice? What resources do you use to find the diet specific information?
Reflective and clarifying questions	
Reflective questioning; Seeking clarification; Asking for more information	You said that you had to 'avoid certain foods.' What foods did you avoid and why? How did this make you feel?You talked about . . . (e.g. having to change your diet, not being able to socialise in relation to food). How did that make you feel?What did you do in that situation?Can you tell me more about what you did at that time?
Interview closure	Is there anything else that you would like to add or talk about in relation to food, nutrition, eating and drinking?

Table 2 Process of data analysis using Colaizzi's framework

Steps of data analysis	Activities involved
Step 1	All transcripts were read by one researcher (WCD) to acquire familiarity with the data and to gain a broad understanding of the issues covered The transcripts were anonymised and pseudonyms given to study participants. All other names of individuals or institutions mentioned during the interview were replaced by a professional or personal relationship status (e.g. 'gastroenterologist', 'IBD nurse', 'hospital', 'wife', 'boyfriend', etc.)
Step 2	Using an inductive process, significant words and statements relating to the topic of the study were identified from the first six transcripts and a list of codes created independently by two researchers (WCD and MM)
Step 3	The two researchers (WCD and MM) met to discuss and formulate the meaning for the identified codes and statements. Any differences were explored and were resolved by discussion and review of the transcripts
Step 4	According to their meaning, the list of codes and statements was preliminarily ordered into themes and the consensus was reached by discussion (WCD and MM) The list of themes was further discussed with a third researcher (KW), who also read six randomly selected transcripts, to clarify the meaning and to identify any overlap. Any overlapping or repetitious codes were combined. These resulted in creation of five emerging themes and several sub-themes The newly created structure was used to code all 28 transcripts using NVIVO, version 11, by the same researcher (WCD). There was no need to create new main themes
Step 5	Two researchers (WCD and MM) met to discuss the themes and the data allocated to each of the themes and sub-themes. The coded data were re-read to verify the meaning and the theme allocation. At this point, all transcripts were re-read to double check that all collected data was reflected in the themes created. This resulted in some of the smaller sub-themes being amalgamated
Step 6	All of the resulting ideas were integrated into a detailed description of the identified issues. As a result of word limits, data were presented under the main themes only, utilising the range of direct quotes from participants' interviews All the team members read the data summary and provided comments on the draft of the results. Further data reduction and/or clarification, retaining the original data meaning, resulted in re-drafting of the paper
Step 7	All the study researchers read and commented on the final draft

The study was approved by the South West Frenchay National Research Ethics Committee (Ref: 11/DW/0291). A participant information sheet was provided to interested participants and all were given sufficient time to consider their participation. Those interested in participation provided their written informed consent.

Participants were reminded that the interviewer (LDH) had no direct involvement in their care. The principles of confidentiality and anonymity were applied throughout the study by giving participants pseudonyms and deleting any data (e.g. hospital name, consultant name, geographical location) that may have led to individuals being identified.

Results

Study participants

Of 48 eligible patients who expressed an interest in participation, 28 (57.1%) were subsequently interviewed. Reasons for not interviewing included: being unable to arrange a convenient time ($n = 5$), patients changing their minds ($n = 5$) and nonresponse to follow-up contact ($n = 10$). Twenty-eight patients with IBD were interviewed: 16 CD (nine female) and 12 UC (six female). Participants' demographic and clinical data are presented in Table 3. The median time since diagnosis was 7 years, with 10 diagnosed for ≤4 years, eleven for 5–10 years and seven for over ≥11 years. The interview time ranged from 29 to 91 min depending on the detail of respondents' accounts. There were no noticeable differences of food experience between people with CD and UC; therefore, the results are presented together for these two groups.

Study themes

Five themes were identified from the data, each containing several sub-themes (Table 4). For succinctness, the data are presented under the main themes only, incorporating all the sub-themes. Direct participants' quotes are presented in italic with the participant's identifiers of pseudonym, gender, age and diagnosis.

Table 3 Demographic and clinical data of the 28 study participants with inflammatory bowel disease

	Crohn's disease ($n = 16$)	Ulcerative colitis ($n = 12$)
Sex, *n* (%)		
Male	7 (44.7)	6 (50)
Female	9 (56.3)	6 (50)
Age (years), mean (SD)	37.6 (10.9)	37.3 (12.5)
Duration of diagnosis (years), mean (SD)	10.3 (10.9)	10.4 (10.8)
Active disease (self-report), *n* (%)	9 (56.3)	4 (25)
Previous IBD surgery, *n* (%)	7 (43.8)	1 (8.3)
Body mass index, mean (SD)	23.3 (5.9)	23.2 (5.7)
MUST category, *n* (%)		
Low risk	10 (63.6)	6 (50)
Medium risk	3 (18.2)	5 (41.7)
High risk	3 (18.2)	1 (8.3)

MUST, Malnutrition Universal Screening Tool.

Table 4 Themes and sub-themes from semi-structured interviews with 28 people with inflammatory bowel disease relating to food, nutrition, eating and drinking in inflammatory bowel disease (IBD)

Theme 1: Personal experience of relationship between IBD and food
IBD symptoms and impact on food intake
Impact of food intake on IBD symptoms
Theme 2: Managing diet to control IBD and its symptoms
'Experimenting' with food intake to manage symptoms
Food avoidance, food exclusion and food substitution
'Bad' food and 'good' food
Frequency of eating, portion sizes and planning ahead
Healthy eating, vitamins and minerals
Eating preferred food and dealing with the consequences
Theme 3: Impact of food-related issues on everyday life
Being organised, shopping, recipes and food preparation
Impact on family, personal and professional life
Social occasions and eating out
Theme 4: Acceptance and normalisation of food and its impact in IBD
Accepting new situation and 'normalisation'
Being in control
Missing the pleasure of being unrestricted about eating and drinking
Theme 5: Sources of information and support
Not knowing enough
Conflicting information regarding food in IBD
Health professionals, family and friends as sources of information and support
Limited sources of information and support

Personal experience of relationships between inflammatory bowel disease and food

Participants made a direct link between IBD diagnoses and associated symptoms, with the impact being their perceived dietary restrictions. Equally, participants talked extensively about their perceived relationship between the food they consume and the presence or severity of the IBD symptoms.

Many participants reported loss of appetite as the main problem related to their IBD: *My appetite is one of the first things to go during a flare. So that's the most noticeable thing. I won't feel hungry at all, I can go pretty much all day without eating anything* (Kush, M, 18, CD). Other symptoms, such as abdominal pain, diarrhoea, bloating, mouth ulcers and loss of taste, also affected diet, particularly when IBD symptoms were more severe: *When your IBD is flaring and you are not well, you just don't want to eat, you just don't want any food to touch your lips* (Tessa, F, 63, CD) but returning to normal diet when well: *If I'm having no symptoms or flare-up, it's not bad, and I can eat absolutely anything* (Amanda, F, 35, UC). There were

some participants who made no change to their diet as a result of their IBD diagnosis: *There's nothing in my UC that makes me eat differently . . . I don't schedule my eating in any form at all to do with UC* (Andrew, M, 44, UC) and others that constantly tried to judge the interaction between their IBD symptoms and making decisions regarding what to eat: *It feels like my body is telling me what's not good for me* (Beth, F, 35, CD).

Factors related to medical and surgical treatments affected participants' decisions about whether and what to eat. For example, the increased appetite during steroid treatment was often a period of when participants felt unrestricted about their diet, despite the greater severity of their IBD symptoms: *If I'm on steroids that definitely affects what I eat. So I eat more. But for me at that time it's usually a good thing because I've usually lost a lot of weight* (Paul, M, 25, CD). However, some were also concerned about the negative effects of overeating on excessive weight gain as a result of steroids. IBD-related surgery (e.g. stoma, ileo-anal pouch, anastomosis), surgery-related complications or intestinal strictures were reported by participants as impacting on their food consumption: *Since surgery, foods are trial and error . . . I do have bouts of pouchitis and bleeding and stuff occasionally. So that took a bit of getting used to, because I could just eat anything before the bowel was removed and then realising afterwards that certain foods like salad and fruit, I can eat them now, but I wasn't retaining anything. It would just come out solid* (Stephan, M, 42, UC).

Participants talked about altering their diet as a direct effect of IBD: *Before [IBD], I never thought about not eating certain types of food, just when [since] I had the colitis* (Stephan, M, 42, UC). The perceived close link between IBD symptoms, frequency of going to the toilet and food, created negative emotions: *I think because you're going to the toilet all the time you're not holding down food, then you get scared to eat . . . It got to the point where I was nervous and you get that nervous tummy and I was going to the toilet a lot, then I'd just stop eating* (Ellen, F, 32, CD).

Food was not seen as a direct reason for causing a flare, although it was linked with symptom deterioration during active disease: *No, I don't think what I eat actually contributes to the flare-up, I don't think it causes it, but I think when I'm having a flare-up, what I eat can certainly exacerbate the flare-up* (Esther, F, 38, UC). Participants talked about certain foods, or a group of foods, as a trigger exacerbating their IBD symptoms. The specific trigger foods varied widely between individuals, including spicy foods, high-fat foods, red meat, dairy products, fruit, vegetables, alcohol, coffee and fizzy drinks, and the symptoms exacerbated by food consumption included pain, diarrhoea, bloating, frequency and urgency, nausea and vomiting, and a feeling of heaviness and fatigue. Some participants linked these symptoms with a particular food: *I've noticed that sometimes there are certain things that I eat will aggravate, like spicy foods . . . After I've eaten something spicy, the next morning I'm just on the toilet a lot* (Anna, F, 17, CD), whereas others perceived eating in general as triggering their symptoms: *Nothing really affected it [symptoms] that I could pinpoint then because it was literally everything, everything that went past my mouth . . . even a sip of water . . . or a bite of biscuit would send me running to the toilet* (Catherine, F, 37, UC). Some participants linked symptoms to the portion size (larger portion) or the frequency of eating (irregular meals). However, there were also some participants who did not specifically link food or eating with IBD symptoms: *I mean if you'd eaten a load and then you had to go [defecate] quickly . . . I think that's more like a general symptom anyway* (Martha, F, 29, UC).

Managing diet to control inflammatory bowel disease and its symptoms

Although participants' reported food and eating exacerbated their IBD symptoms, they commonly tried to unravel this relationship and used diet to manage their symptoms: *There was clearly something wrong and the obvious cause for this was something that I eat. So what can I do other than removing certain things to see if it has an effect, adding certain things to see if it has an effect* (Andrew, M, 44, UC). The methods most frequently used were food restrictions, food exclusion, food substitution and changing food preparation, all of which required constant planning. All participants talked about experimenting with food by excluding 'bad foods' and replacing it with 'good foods'. However, the list of bad foods and good foods differed between participants and was influenced by perceived food intolerance or the exacerbating IBD symptoms.

Opinions regarding healthy eating were widely polarised, with some trying to follow the advice of health professionals to increase intake of fruit, vegetables, fibre and having a balanced diet, whereas others were questioning the meaning of healthy diet in IBD: *Knowing what a healthy diet is and realising that's not going to be particularly healthy at that point in time for me from a colitis point of view* (Adam, M 41, UC). Intake of fibre was increased by some, whereas others did the opposite: *The only change I have made now is that I don't eat a lot of fibre. I used to have wholemeal bread, brown rice, brown pasta, etc., but now I have white instead because I know that having a lot of fibre makes you go to the toilet more* (Catherine, F, 37, UC). For participants who had vitamin and mineral deficiencies or were underweight, a healthy

diet was interpreted as one that helped them to gain weight: *I was massively underweight, and I did see a dietitian for a little bit, but we didn't look at what kind of foods were making me worse or better . . . I was just eating everything and anything, it's just that I've been trying to put weight on* (Thomas, M, 25, CD).

All participants talked about experimenting with food by either following an exclusion diet and then slowly reintroducing the excluded products, cooking very plain food, mashing or liquidising food, which they perceived made it easier to digest. Often, participants did not follow the changes for any specified period of time or did not keep a food/symptom diary to record how effective the changes were. In most cases, this was not done under the supervision of a healthcare professional but was down to a participant's own experimentation. There were some participants who followed a severely restricted and limited diet in the belief that there will be fewer foods to exacerbate symptoms. In others, food choice was based on their likes and dislikes because they preferred to have enjoyment of food and if necessary to deal with consequences of having to go to the toilet more frequently. Many participants talked about knowing or anticipating unpleasant outcomes (e.g. abdominal pain, increased stool frequency) but persevered with eating particular food(s) because they had denied themselves this pleasure for so long.

Eating frequent and regular meals, eating slowly and a small to moderate portion size were all used as possible methods to limit the negative impact of food on IBD symptoms: *I'm trying to eat four or five times a day – smaller amount. It's better for me* (Beth, F, 35, CD), whereas some try to avoid eating altogether: *If my stomach's playing up, so normally I would starve my stomach so that there's nothing in it. Sometimes I don't eat the whole day* (Ellen, F, 32, CD).

Impact of food-related issues on everyday life

The food-related issues described (personal experience of IBD and food, managing diet to control IBD and symptoms) impacted patients' everyday life. For participants to be able to 'get on' with their life, they had to plan many activities in advance, from going food shopping, food preparation, through to work, hobbies and socialising.

As a result of actual or perceived food restrictions related to IBD, food shopping (e.g. checking ingredient labels) and food preparation was more time consuming: *I'd look on the labels to make sure I didn't think it would upset me* (Jalal, M, 51, CD). Participants perceived food preparation to be more burdensome: *It's the cooking that sometimes really upsets me because I have to cook twice* (Mary, F, 56, CD), whereas others used more flexible methods such as separating food for themselves before spices or certain ingredients were added for family members (e.g. onion, garlic).

Depending on how restrictive or varied the type of food and the recipes were, participants found differing levels of support from their partners and family members, with some being more willing to compromise, whereas, for others, mealtimes resulted in conflict or not eating together: *Everybody else in the house was continuing with their normal diets and I would usually end up eating separately* (Kush, M, 18, UC). One participant felt that she had to be a positive role model and give a good example to her daughter: *it's not just myself that I'm eating, you know planning meals for. It's also making sure that my child has a healthy concept of food and a healthy relationship with food* (Ester, F, 38, UC).

Some participants reported food-related issues and the effect on their symptoms as impacting on their daily functioning. Needing to visit a toilet soon after eating created anxiety for some: *I'm a bit scared to eat because I know I'm going to need to run to the toilet* (Beth, F, 35, CD). The work environment created very specific challenges to people with IBD. Some tried to be organised and plan ahead and to take their lunch to work to give themselves as much control as possible: *It's nice to know that there are things that I can eat, that are there available to me when I want it* (Dahlia, F, 22, CD). Others would eat less or avoid eating all together: *A big part of it is my eating habits, because when I'm at work I don't eat, because I know if I eat I have to go to the loo . . . If I knew I had to be out all day, I probably would consciously eat less the day before* (Thomas, M, 25, CD). Where possible, some participants tried to work from home because this way they felt unrestricted about the frequency of eating at the same time as being close to the toilet. Other strategies to manage IBD symptoms also created problems for some in the work environment (e.g. more frequent meal breaks, avoiding specific foods), as a result of a lack of understanding among their colleagues: *I feel like they are looking and, "Oh she's eating again", you know. I think they don't understand. They know that I have this disease but they don't know how it affects me* (Beth, F, 35, CD). Some female participants reported feeling faced with suspicion if they were not drinking alcohol at work events: *If you're a woman and you're not drinking, people start making assumptions, "Oh is she pregnant and is it going to impact on her career?"* [Janet, F, 29, UC].

Social lives were greatly impacted, in a wide variety of ways, by having IBD and food restrictions. For some, symptoms associated with eating, particularly higher frequency of visiting the toilet, needing a toilet during a meal and pain after eating, were strong deterrents from going out and socialising: *It's awkward when, if you're at a restaurant and all of a sudden you have to bolt to wherever the*

toilet might possibly be (Gary, M, 30, CD). Many of the study participants felt nervous about eating out in new places because they were apprehensive about unfamiliar menus and certain food ingredients that they may be intolerant of: *Before I go, I really study the menu and see what to have* (Mary, F, 56, CD). For some, going out to eat was part of carefully planned exercise rather than a spur of the moment decision: *Me and my husband both work. We could go out whenever we want, but we end up at the same few restaurants and I know exactly what I'm going to take before I even walk through the door* (Sandra, F, 41, CD). This reduced the pleasure of going out for some people. Some participants would choose to socialise but would not eat when doing so: *Even if I couldn't eat I was going out anyway just to socialise with my friends* (Dahlia, F, 22, CD), whereas others would refuse 'dinner dates' and find an excuse not to go (e.g. infection, food allergy), so as not to disclose their IBD diagnosis. Special occasions such as birthdays, weddings or festive holidays were perceived by some as difficult and stressful to deal with, whereas others took more relaxed approach and were prepared to experience the symptoms that celebratory eating would cause. Those who had more experience of living with IBD felt better able to cope with different situations: *If a friend is going to take offence because I don't eat the full portion, then that's their problem* (Katy, F, 47, CD).

Some, who were unable to drink alcohol, felt reluctant to go out to social events where alcohol was involved because they thought that that they would ruin enjoyment of others, or feel pressure from others to conform: *I went to my friend's birthday when I was very much off alcohol and, they were saying 'Oh go on, have a glass of wine.' I know that it was much more important for me not to* (Janet, F, 29, UC), whereas some were resilient to the social pressure of drinking: *Alcohol doesn't rule my life. I could have it or I could do without. And I prefer to do without it . . . If I actually go into a pub, with my wife or with a couple of friends, they have alcohol and I have orange juice* (Robert, M, 59, UC).

Acceptance and normalisation of food and its impact in inflammatory bowel disease

Many participants talked about negative emotions linked with the psychosocial impacts of food, nutrition, eating and drinking with IBD, including stress, annoyance, frustration and low mood.

Acceptance of IBD diagnosis and changes to everyday life featured strongly in participants' experiences of food, nutrition, eating and drinking with IBD. This was closely linked with participants trying to normalise their life. For some, normalisation was expressed by eating 'normal food' and trying to live their life as before their diagnosis, trying to ignore their IBD diagnosis and trying to cope with a higher frequency of going to the toilet: *I don't really like being labelled with it [colitis]. I sort of don't like the pity. I just want to be able to get on with my life and with my job. Not let it interfere in my life, insofar as that is possible* (John, M, 35, UC). Some tried to achieve normalisation by controlling their diet, being careful about what they eat, in hope that this would help them to control the symptoms: *Eating healthier and cutting certain things out hasn't all been bad. Most of it has been good and it makes me feel good knowing that what I'm eating is also good for me and good for my colitis* (Kush, M, 18, UC).

Having control was frequently mentioned and being in control was important for participants. Accepting their condition was seen as a first step to controlling it. However, when participants felt unable to control their disease, they sometimes tried to control their diet: *By making many adjustments to food and drink and general lifestyle as I reasonably can without going completely over the top. That how my life is* (Katy, F, 47, CD). Other forms of control were learning more about what food to eat and what food to avoid, being aware of the environment and where the toilets are, getting to know their body and how it responds to different foods. Hence, a participant's life was based around their IBD and constant thinking about food, its nutritional value and whether or not it will induce symptoms: *I plan everything around my body rather than planning my life then making my body work around it* (Thomas, M, 25, CD). Some participants were prepared to make and accept these changes without *being morbid and dwelling on things* (Esther, F 38, UC), whereas some missed the pleasure of being unrestricted about food and food choices: *I miss having normal diet, I always liked my food and I miss just having what I want* (Catherine, F, 37, UC). They tried to be strong, although they did not manage to succeed all the time, particularly as the restrictions and sacrifices did not always work: *It does vary on a day to day and that's probably the hardest part, because there are times, there are certain things that are going to cause a reaction* (Gary, M, 30, CD). This constant uncertainty only led to more frustration, irritation and doubts in the strategies used.

Sources of information and support

Many participants expressed their limited knowledge and understanding of CD or UC and how diet may affect their condition: *I don't know enough about whether there are differences between normal healthy eating and eating to help colitis* (Janet, F, 29, UC). Hence, they sought help and support about diet in IBD from health professionals. Many participants received diet advice at the time of IBD diagnosis from a gastroenterologist, although the advice frequently consisted mainly of: *It doesn't matter what you*

eat (Tessa, F, 63, CD) because diet is not linked with IBD. Some were more accepting of that advice to continue with their normal diet, whereas others were finding it difficult to accept: *I cannot see how a digestive illness can't have links to food because it just doesn't make sense to me* (Agnes, F, 31, CD).

Most participants were not offered special dietary advice but were told that they could eat everything, whereas others, depending on the presenting symptoms and their severity (e.g. severe abdominal pain or severe weight loss), were referred to a dietitian for advice on an elimination diet, enteral nutrition in CD, low-fibre diet or high-energy diet. Participants' experiences of advice given by dietitians also differed. Some were told to eat *all things in moderation* (Jason, M, 56, CD) and some to restrict their diet at the time of flare, whereas others were told to eat everything and during flare to increase their energy intake. As a result, satisfaction with dietitians' advice and support varied, with some finding it very helpful: *I was in close contact with her (dietitian) and if anything happened, I would just email her* (Dahlia, F, 22, CD) and some finding the advice generic and nonspecific: *It wasn't as helpful as I thought it would be. It's sort of pretty obvious what she said to me really, to stay clear of fibrous food* (Jalal, M, 51, CD). However, some unsuccessfully tried for many years to be referred to a dietitian, and some were of an opinion that if: *My medical doctor told me there's no known correlation, so what would a dietitian tell me?* (Andrew, M, 44, UC). However, many participants did not know what food they should eat or what food to avoid, and if they needed vitamin and mineral supplements.

Only a few participants mentioned dietary support and advice given by IBD specialist nurses. Most of the advice concentrated around principles of healthy eating (e.g. five portions of fruit and vegetable per day).

Some participants thought that health professionals did not take food issues in IBD seriously, or that clinicians were too busy to talk to about diet. Some found the advice superficial, confusing or even conflicting. Hence, participants tried to find diet-related advice by accessing other sources of information, such as seeing dietitians privately, as well as Internet IBD forums and discussion groups. Their satisfaction with information obtained from these sources also varied. Some found the information useful, some thought that they have to find their own way of coping, whereas some talked about increased anxiety regarding food and food restrictions and developed very restrictive dietary habits.

Those participants who disclosed their IBD diagnosis to others found their friends and family to be supportive and understanding. Some of the help and support was more practical (e.g. advice on what to eat or what food to avoid, cooking food that met the individual's preferences) and some was in the form of emotional support: *They don't really say nothing about my weight [being underweight] and that makes me happy because I'm really self-conscious about my weight* (Anna, F, 17, CD). Many participants expressed a wish for a greater support from family and friends; however, their IBD and food-related knowledge was often limited: *My friends know I have Crohn's, but probably a lot of them have never heard about it, so they don't really understand what it is and how it affects me* (Beth, F 35, CD); hence, their advice was not always relevant: *It gets really frustrating when people get confused between irritable bowel and inflammatory bowel, suggesting I go dairy free . . . or to do this or do that . . . I'm there thinking well it doesn't make any difference* (Adam, M, 41, UC).

Discussion

The present qualitative study explores the experience and psychosocial impact of food, nutrition, eating and drinking on the lives of people with IBD. Participants reported close links between IBD and food, in that IBD affected their ability to eat some foods as a result of its impact on symptoms, whereas diet was also used as an approach to manage these symptoms. This bi-directional relationship in most cases had far reaching, negative and compound impacts, requiring restrictions and sacrifices in their private, social and professional lives. Patient-reported experiences of food-related issues in IBD restricting their quality of life are supported by survey data suggesting that 82% of people with IBD experience such problems with food and nutrition [20].

Active disease and the severity of symptoms such as diarrhoea, urgency, abdominal pain, bloating, nausea, vomiting, loss of appetite and mouth ulcers were presented as the main factors affecting participants' food choices. Participants restricted the range of foods consumed, completely excluded some foods, reduced the amount or frequency of eating, or all of these, in attempts to adapt their life to their IBD. These behaviours may contribute to nutritional problems frequently reported in IBD, including micronutrient deficiencies, malnutrition and even being overweight. Between 20% and 85% of people with IBD have been reported as being at risk of malnutrition [21,22]. Malnutrition is associated with suboptimal health outcomes [23], reduced quality of life [4], fatigue [24] and diminished strength [25].

Even during IBD remission, participants observed that certain symptoms (e.g. abdominal pain, diarrhoea, bloating, frequency and urgency, nausea and vomiting, heaviness and fatigue) were exacerbated by eating in general, or by certain food groups, or by spicy or fatty food. At

the same time, the presence of these physical symptoms affected participants' appetites and made them anxious about eating. It could be argued that presence of gastrointestinal symptoms during remission may indicate the presence of functional, rather than inflammatory symptoms [12,26]. However, the aim of the present study was to explore the perceptions and psychosocial impacts of food, nutrition, eating and drinking on the lives of people with IBD, and this was irrespective of whether the experiences resulted from symptoms that were the result of active disease, functional gut symptoms, both, or neither. Interestingly, a previous qualitative study investigated the experiences of eating among eight women with either IBS (i.e. functional symptoms alone) or IBD. Although few comparisons were made between the two conditions, similar experiences were identified to those reported in the present study (i.e. healthy eating, trigger foods, dietary restrictions, control, support from family and friends) [12–14].

There are wide ranges of prevalence of functional gut symptoms reported in IBD, mainly as a result of heterogeneity and challenges with respect to defining them [26]; however, the pooled prevalence of those satisfying definitions of IBS in IBD was 39% (44% in active, 35% in remission) [27]. This suggests that over one-third of IBD patients could be considered for optimising functional gut symptom management, which may include modification of diet, lifestyle, psychological and pharmacological treatments [28]. Dietary approaches to managing functional gut symptoms in IBD include the low FODMAP diet, which has some supportive evidence from both uncontrolled [20] and controlled studies [29–31]. The term FODMAP is an acronym for Fermentable Oligo-, Di-, Monosaccharides And Polyols, comprising short chain carbohydrates that are poorly absorbed in the small intestine [32]. Although improved research on the efficacy of the low FODMAP diet is required, patients in the present study frequently reported foods high in fructans (e.g. onions, garlic) to be associated with abdominal pain, bloating and diarrhoea and this has been confirmed in re-challenge studies in IBD [30]. If patients' complaints of functional gut symptoms reported during remission are ignored or not formally evaluated by clinicians, this may result in a lack of trust between the patient and clinician, and lead patients to seek information elsewhere and/or develop adverse behaviours with restrictive diet habits that may be nutritionally inadequate [13,20,33–35].

Participants did not link their IBD diagnosis or any relapses to their diet. However, they were strongly of the opinion that they could use diet as a means to manage their symptoms. Similar views are found in the literature, where diet is reported to influence intestinal inflammation (e.g. altering the gut microbiome), although with scarce evidence that diet alters the natural history of IBD [7,36–41]. Food restrictions and exclusions, as well as experimenting with food by trial and error, were reported by participants as methods frequently used to control their IBD symptoms. Participants found these methods practically challenging in terms of shopping, cooking and finding recipes, and this caused many emotional challenges in terms of them being able to socialise, take part in special occasions and enjoy food in the same way as before the IBD diagnosis. Similar issues have been reported in previous studies [35,40].

Participants talked about having to plan their daily activities in advance, and constantly needing to think about what and where to eat, as well as having to consider access to toilets. This constant planning and restriction created stress and anxiety, and contributed to diminished enjoyment of food and everyday life. Many participants felt that they had lost control of their lives and that they were leading more restrictive and limited lives. Consumption of food and alcohol is at the centre of many peoples' social life and the consumption of certain types of food is often culturally driven. Making changes to the type of food consumed or avoiding certain foods and alcohol may contribute to changes in the individual's emotions and their enjoyment of food [37,42]. Patients decisions regarding food choice may vary depending upon their primary aim (e.g. symptom control, social engagement, participation in cultural celebrations, food enjoyment) and this therefore requires constant planning, creating at times, internal or external conflicts. Diet and diet manipulation, such as food avoidance, food restriction and food substitution, were perceived by participants as a way of controlling their everyday life. Being in control of their body, IBD symptoms and their life at large was the ultimate goal, which participants tried to achieve on a daily basis.

Access to information on IBD and diet was seen as an important avenue to equip them with knowledge and achieve better control. However, a lack of reliable sources, good quality information and limited guidance and support from health professionals left participants struggling to find effective management strategies [14,43,44]. Most of the management strategies reported by participants related to making restrictions to their diet (identifying trigger foods by trial and error, food restrictions or avoidance and its reintroduction) or their private, social and professional lives, or both. Some of the strategies were positive (e.g. following healthy and balanced diet, avoiding certain foods during a flare but returning to normal diet during remission, taking part in social life), although many were negative, with extensive food exclusions over a prolonged period of time, leading to frustration, irritation and a lack of enjoyment of food.

It is unclear which factors may play a role in developing positive or negative coping strategies [18,41,45]. Exploring the factors and having a better understanding of the adaptation process would help to provide the guidance and support required to help people with IBD overcome their physical and emotional food-related problems. Greater emphasis should be placed on assessing and addressing food-related quality of life in IBD aiming to identify the extent and severity of the problem, the impact on patients' diet and nutrition and the wider impact on their life. A food-related quality of life questionnaire has been specifically developed and validated in IBD [46]. This questionnaire should help to reflect the impact of IBD on individual's food-related quality of life, instigate the provision of help and advice specific to an individual's needs and also help to facilitate the process of acceptance and positive adaptation.

Although there is a wealth of evidence of specific diets being used in different patients groups, such as nutritional deficiencies, malnutrition and strictures;[6,33,47–50] sources of information for patients helping them to maintain their healthy and balanced diet during remission are limited [43,51–53]. Participants in the present study were frequently advised by health professionals that there is no evident link between IBD and diet. This perhaps relates to the limited evidence for the role of specific foods in the pathogenesis of IBD onset [48,49] and the lack of effectiveness of diet in the management in UC [47,54]. However, there is a disconnect between health professionals' advice regarding the lack of effect of diet in IBD and patients' everyday experiences of eating and drinking with IBD. This contradictory dynamic between advice from health professionals and an individual's own beliefs about the role of diet in IBD may leave patients feeling that their food-related concerns are ignored by their clinicians. Although participants indicated that the advice from health professionals was often provided by dietitians, the whole multidisciplinary team, including gastroenterologists and IBD specialist nurses, should understand the impact of IBD on eating and drinking with respect to advising and supporting patients.

Strengths and limitations of the study

The qualitative design of the study 'gave voice' to people diagnosed with IBD and allowed for an in-depth exploration of their experience of how IBD is affecting their perceptions and psychosocial impact of food in their lives. A benefit of using semi-structured interviews is that this sets the boundaries of the topic and the direction of the conversation compared to an unstructured approach. The limitations of qualitative research are that it involves a small number of participants and the findings relate predominantly to these individuals. Although the main aim of qualitative research is to provide an in-depth description of the study participants experience, it is nevertheless expected that the findings will be transferable to similar contexts, which, in this case, comprise participants with similar clinical and demographic characteristics [55]. Greater effort needs to be directed towards recruiting participants from more diverse ethnic and cultural backgrounds. The use of semi-structured interviews may restrict the participants to primarily cover the topic set out by the interview guide, instead of covering all of the aspects related to their experience. This limitation was partly off-set by a conversational style and 'unrestricted' interview time, allowing the participants to express their experience and issues of importance to them more fully.

Conclusions

Food-related quality of life in IBD patients was reported to be negatively affected across a variety of psychosocial aspects of life; however, the scale of the problem needs further exploration. A variety of approaches for altering diet were used in an attempt to find an optimal way to function. However, insufficient information or a lack of support from health professionals resulted in many participants feeling trapped into using a trial and error cycle as a preliminary coping strategy. Patients with IBD need diet and life style advice that will help them to make positive adjustments. Currently, there is insufficient evidence on what that advice should be and hence further research is recommended to explore patients' exact needs.

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Conflict of interests, source of funding and authorship

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KW, JOL, MCL and MM were responsible for the study conception. KW, JOL, MCL, MM and LDH were responsible for the study design. LDH was responsible for data collection. WCD and MM were responsible for data analysis and interpretation. WCD and KW were responsible for drafting the manuscript. All authors approved the final version of the manuscript submitted for publication.

Transparency declaration

The lead author affirms that this manuscript is an honest, accurate and transparent account of the study being reported. The reporting of this work is compliant with COREQ guidelines. The lead author affirms that no important aspects of the study have been omitted and that there were no discrepancies from the study as planned and the study was approved by the South West Frenchay National Research Ethics Committee (Ref: 11/DW/0291).

References

1. Bernstein CN, Fried M, Krabshuis J *et al.* (2010) World gastroenterology organization practice guidelines for the diagnosis and management of IBD in 2010. *Inflamm Bowel Dis* **16**, 112–124.
2. Cohen R (2002) The quality of life in patients with Crohn's disease. *Aliment Pharmacol Ther* **16**, 1603–1609.
3. Ghosh S & Mitchell R (2007) Impact of inflammatory bowel disease on quality of life: results of the European Federation of Crohn's and Ulcerative Colitis Associations (EFCCA) patient survey. *J Crohns Colitis* **1**, 10–20.
4. Norman K, Kirchner H, Lochs H *et al.* (2006) Malnutrition affects quality of life in gastroenterology patients. *World J Gastroenterol* **12**, 3380–3385.
5. Day A, Whitten K, Sidler M *et al.* (2008) Systematic review: nutritional therapy in paediatric Crohn's disease. *Aliment Pharmacol Ther* **27**, 293–307.
6. Hartman C, Eliakim R & Shamir R (2009) Nutritional status and nutritional therapy in inflammatory bowel diseases. *World J Gastroenterol* **15**, 2570–2578.
7. Lewis JD & Abreu MT (2017) Diet as a trigger or therapy for inflammatory bowel diseases. *Gastroenterology* **152**, 398–414.
8. Prince A, Moosa A, Whelan K *et al.* (2010) Nutrition problems and research priorities of patients with Crohn's disease and ulcerative colitis. *J Hum Nutr Diet* **23**, 460–461.
9. Lomer M, Hart A, Verjee A *et al.* (2017) What are the dietary treatment research priorities for inflammatory bowel disease? A short report based on a priority setting partnership with the James Lind Alliance. *J Hum Nutr Diet* **30**, 709–713.
10. Gustafsson U & Draper A (2009) The social aspects of food and nutrition. *J Hum Nutr Diet* **22**, 87–88.
11. Coveney J (1999) *Food, Morals and Meaning: The Pleasures and Anxiety of Eating*. London: Routledge.
12. Fletcher PC & Schneider MA (2006) Is there any food i can eat?: Living with inflammatory bowel disease and/or irritable bowel syndrome. *Clin Nurse Spec* **20**, 241–247.
13. Jamieson AE, Fletcher PC & Schneider MA (2007) Seeking control through the determination of diet: a qualitative investigation of women with irritable bowel syndrome and inflammatory bowel disease. *Clin Nurse Spec* **21**, 152–160.
14. Fletcher PC, Jamieson AE, Schneider MA *et al.* (2008) "I know this is bad for me, but . . .": a qualitative investigation of women with irritable bowel syndrome and inflammatory bowel disease: Part II. *Clin Nurse Spec* **22**, 184–191.
15. Jones R, Hunt C, Stevens R *et al.* (2009) Management of common gastrointestinal disorders: quality criteria based on patients' views and practice guidelines. *Br J Gen Pract* **59**, e199–e208.
16. UK Inflammatory Bowel Disease Audit Steering Group. (2009). *UK IBD Audit 2008 (Executive Summary)*. London: Royal College of Physicians.
17. Moosa A, Prince A, Reidlinger D *et al.* (2010) Patients and dietitians report variable access to quality written dietary information regarding inflammatory bowel disease. *J Hum Nutr Diet* **23**, 456–457.
18. Palant A, Koschack J, Rassmann S *et al.* (2015) "And then you start to loose it because you think about Nutella": the significance of food for people with inflammatory bowel disease – a qualitative study. *BMC Gastroenterol* **15**, 93.
19. Colaizzi P (1978) Psychological research as a phenomenology views it. In: *Existential Phenomenological Alternatives for Psychology*. pp. 48–71 [Valle R & King M, editors]. New York, NY: New York University Press.
20. Prince A, Whelan K, Moosa A *et al.* (2011) Nutritional problems in inflammatory bowel disease: the patient perspective. *J Crohns Colitis* **5**, 443–450.
21. Goh J & O'morain C (2003) Nutrition and adult inflammatory bowel disease. *Aliment Pharmacol Ther* **17**, 307–320.
22. Lomer MC (2011) Dietary and nutritional considerations for inflammatory bowel disease. *Proc Nutr Soc* **70**, 329–335.
23. White JV, Guenter P, Jensen G *et al.* (2012) Consensus statement of the academy of nutrition and dietetics/american society for parenteral and enteral nutrition: characteristics recommended for the identification and documentation of adult malnutrition (undernutrition). *J Acad Nutr Diet* **112**, 730–738.

24. Hengstermann S, Valentini L, Buening C *et al.* (2006) Malnutrition in quiescent inflammatory bowel diseases cannot be diagnosed with standard tools. *Gastroenterology* **130**, A217–A218.
25. Valentini L, Schaper L, Buning C *et al.* (2008) Malnutrition and impaired muscle strength in patients with Crohn's disease and ulcerative colitis in remission. *Nutrition* **24**, 694–702.
26. Teruel C, Garrido E & Mesonero F (2016) Diagnosis and management of functional symptoms in inflammatory bowel disease in remission. *World J Gastrointest Pharmacol Ther* **7**, 78–90.
27. Halpin SJ & Ford AC (2012) Prevalence of symptoms meeting criteria for irritable bowel syndrome in inflammatory bowel disease: systematic review and meta-analysis. *Am J Gastroenterol* **107**, 1474–1482.
28. Major G & Spiller R (2014) Irritable bowel syndrome, inflammatory bowel disease and the microbiome. *Curr Opin Endocrinol Diabetes Obes* **21**, 15–21.
29. Pedersen N, Andersen NN, Végh Z *et al.* (2014) Ehealth: low FODMAP diet vs lactobacillus rhamnosus gg in irritable bowel syndrome. *World J Gastroenterol* **20**, 16215–16226.
30. Cox SR, Prince AC, Myers CE *et al.* (2017) Fermentable carbohydrates [FODMAPS] exacerbate functional gastrointestinal symptoms in patients with inflammatory bowel disease: a randomised, double-blind, placebo-controlled, cross-over, re-challenge trial. *J Crohns Colitis* **11**, 1420–1429.
31. Cox SR, Stagg AJ, Fromentin S *et al.* (2018) *Low FODMAP Diet Improves Functional-Like Gastrointestinal Symptoms but Reduces Bifidobacteria and Faecalibacterium Prausnitzii in Quiescent Inflammatory Bowel Disease: A Randomised Controlled Trial and Metagenomic Analysis*. Vienna: European Crohn's and Colitis Organisation.
32. Whelan K, Martin LD, Staudacher HM *et al.* (2018) The low FODMAP diet in the management of irritable bowel syndrome: an evidence-based review of FODMAP restriction, reintroduction and personalisation in clinical practice. *J Hum Nutr Diet* **31**, 239–255.
33. Haskey N & Gibson DL (2017) An examination of diet for the maintenance of remission in inflammatory bowel disease. *Nutrients* **9**, 259.
34. Staudacher HM, Kurien M & Whelan K (2018) Nutritional implications of dietary interventions for managing gastrointestinal disorders. *Curr Opin Gastroenterol* **34**, 105–111.
35. Tomar SK, Kedia S, Upadhyay AD *et al.* (2017) Impact of dietary beliefs and practices on patients with inflammatory bowel disease: an observational study from India. *JGH Open* **1**, 15–21.
36. Cabré E & Domènech E (2012) Impact of environmental and dietary factors on the course of inflammatory bowel disease. *World J Gastroenterol* **18**, 3814–3822.
37. Zallot C, Quilliot D, Chevaux J-B *et al.* (2012) Dietary beliefs and behavior among inflammatory bowel disease patients. *Inflamm Bowel Dis* **18**, 2232–2239.
38. Hou JK, Lee D & Lewis J (2014) Diet and inflammatory bowel disease: review of patient-targeted recommendations. *Clin Gastroenterol Hepatol* **12**, 1592–1600.
39. Uranga JA, López-Miranda V, Lombo F *et al.* (2016) Food, nutrients and nutraceuticals affecting the course of inflammatory bowel disease. *Pharmacol Rep* **68**, 816–826.
40. Cohen AB, Lee D, Long MD *et al.* (2013) Dietary patterns and self-reported associations of diet with symptoms of inflammatory bowel disease. *Dig Dis Sci* **58**, 1322–1328.
41. Limdi JK, Aggarwal D & McLaughlin JT (2016) Dietary practices and beliefs in patients with inflammatory bowel disease. *Inflamm Bowel Dis* **22**, 164–170.
42. Lindsay J (2010) Healthy living guidelines and the disconnect with everyday life. *Critical Public Health* **20**, 475–487.
43. Prince AC, Moosa A, Lomer MC *et al.* (2015) Variable access to quality nutrition information regarding inflammatory bowel disease: a survey of patients and health professionals and objective examination of written information. *Health Expect* **18**, 2501–2512.
44. Holt D, Strauss B & Moore G (2017) Patients with inflammatory bowel disease and their treating clinicians have different views regarding diet. *J Hum Nutr Diet* **30**, 66–72.
45. Livneh H (2001) Psychosocial adaptation to chronic illness and disability a conceptual framework. *Rehabil Couns Bull* **44**, 151–160.
46. Hughes LD, King L, Morgan M *et al.* (2015) Food-related quality of life in inflammatory bowel disease: development and validation of a questionnaire. *J Crohns Colitis* **10**, 194–201.
47. Rajendran N & Kumar D (2010) Role of diet in the management of inflammatory bowel disease. *World J Gastroenterol* **16**, 1442–1448.
48. Scholz D (2011) The role of nutrition in the etiology of inflammatory bowel disease. *Curr Probl Pediatr Adolesc Health Care* **41**, 248–253.
49. Lee D, Albenberg L, Compher C *et al.* (2015) Diet in the pathogenesis and treatment of inflammatory bowel diseases. *Gastroenterology* **148**, 1087–1106.
50. Owczarek D, Rodacki T, Domagała-Rodacka R *et al.* (2016) Diet and nutritional factors in inflammatory bowel diseases. *World J Gastroenterol* **22**, 895–905.
51. Zhou Y, Ma X & Chen Y (2014) Dietary practices of Chinese patients with inflammatory bowel disease: a naturalistic inquiry. *Gastroenterol Nurs* **37**, 60–69.
52. Vagianos K, Clara I, Carr R *et al.* (2016) What are adults with inflammatory bowel disease (IBD) eating? A closer look at the dietary habits of a population-based Canadian IBD cohort. *J Parenter Enteral Nutr* **40**, 405–411.

53. Opstelten JL, de Vries JH, Wools A *et al.* (2018) Dietary intake of patients with inflammatory bowel disease: a comparison with individuals from a general population and associations with relapse. *Clin Nutr*, in press. https://doi.org/10.1016/j.clnu.2018.06.983
54. Jowett S, Seal C, Pearce M *et al.* (2004) Influence of dietary factors on the clinical course of ulcerative colitis: a prospective cohort study. *Gut* **53**, 1479–1484.
55. Malterud K (2001) Qualitative research: standards, challenges, and guidelines. *Lancet* **358**, 483–488.

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INFLAMMATORY DISORDERS

Metabolic syndrome and its association with the Dietary Inflammatory Index (DII)® in a Croatian working population

G. Kenđel Jovanović,[1] S. Pavičić Žeželj,[1] S. Klobučar Majanović,[2] I. Mrakovcic-Sutic[3] & I. Šutić[4]

[1]Department of Health Ecology, Teaching Institute of Public Health of Primorsko-Goranska County, Rijeka, Croatia
[2]Department of Endocrinology, Diabetes and Metabolic Diseases, Clinical Hospital Centre Rijeka, Rijeka, Croatia
[3]Department of Physiology, Immunology and Pathophysiology, Faculty of Medicine, University of Rijeka, Rijeka, Croatia
[4]Department of Family Medicine, Faculty of Medicine, University of Rijeka, Rijeka, Croatia

Keywords
Croatia, diet, Dietary Inflammatory Index (DII)®, metabolic syndrome, working population.

Correspondence
G. Kenđel Jovanović, Department of Health Ecology, Teaching Institute of Public Health of Primorsko-Goranska County, Krešimirova 52a, 51000 Rijeka, Croatia.
Tel.: +358 51 358 751
Fax: +385 51 358 753
E-mail: gordana.kendel-jovanovic@zzjzpgz.hr

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Abstract

Background: Metabolic syndrome (MetS) is a global public health concern, although its association with the inflammatory potential of the diet is still indefinite. The main objective of the present study was to investigate the association of MetS and its components with the inflammatory potential of the diet in a Croatian working population with sedentary occupations.
Methods: In a cross-sectional study, Croatian workers (n = 366) self-administrated questionnaires for sociodemographic and health-related data. Their anthropometric measurements and fasting blood samples were collected for evaluation of MetS. The inflammatory potential of the diet was assessed with a Dietary Inflammatory Index (DII)®, scored using dietary data collected from a food frequency questionnaire. Multivariable logistic regression analysis, adjusted for sex, age, body mass index, education, smoking, physical activity and energy intake, was used to establish the association between DII and MetS.
Results: MetS prevalence was 25% and was significantly associated with a pro-inflammatory diet [mean (SD) 3.28 (1.45); $P < 0.01$]. The pro-inflammatory diet was statistically associated with women, university degree, moderate physical activity, snacking between meals, central obesity, hypertriglyceridaemia, hypertension, low high-density lipoprotein-cholesterol, MetS prevalence and lower adherence to a Mediterranean diet. Multivariable logistic regression analysis showed a statistically positive association for a one-unit increase in the DII and MetS prevalence (odds ratio = 2.31; 95% confidence interval = 1.61–3.31; $P < 0.01$) and hypertension (odds ratio = 1.28; 95% confidence interval = 1.01–1.64; $P = 0.04$).
Conclusions: Further longitudinal studies in different parts of Croatia, including inflammation biomarkers, are needed to enable a more defined view of the inflammatory potential of a diet and its association with various inflammatory-based health conditions. The results obtained in the present study indicate the need for the development of anti-inflammatory dietary interventions for population health protection.

Introduction

A multifactorial condition known as the metabolic syndrome (MetS) is a global public health concern [1,2] as a result of its associated risk of cardiovascular disease (CVD), type 2 diabetes, non-alcoholic fatty liver disease and other diseases [3]. Obesity is associated with an inflammation process that can be a precursor for metabolic disease [2], whereas chronic low-grade inflammation may have a great influence on developing MetS [4]. The

most studied dietary pattern in relation to MetS and other diseases is the Mediterranean diet (MD). The MD could decrease inflammation because of its high content of polyphenols, as a result of their high presence in fruits, extra-virgin olive oil, red wine and nuts [5,6]. To estimate the inflammatory potential of an individual's diet, the Dietary Inflammatory Index (DII)® [7] was developed and validated [8] as a scoring algorithm of 45 food parameters. The DII was shown to be a valuable tool for assessing a diet's inflammatory potential. It was investigated in association with MetS, although the results obtained are still not definitive [9–18]. A recent meta-analysis of DII association with the risk of CVD, MetS and mortality revealed that the most pro-inflammatory versus the most anti-inflammatory diet showed no association with an increased risk of MetS [19]. It was assumed that this could be the result of a small number of studies dealing with that association, as well as the different study designs, dietary assessment tools and participant characteristics. The need for further cohort studies in different populations was emphasised to explain that association [19]. A prospective French study [11] and recent cross-sectional Korean [15] and Irish [18] studies found a pro-inflammatory diet to be associated with MetS prevalence, whereas other similar studies [9,10,12–14,16,17] did not report any association. However, DII was related to MetS or its components in five studies [10,16,18,20,21]. Among the Croatian population, MetS investigations are sparse, mostly having been conducted among populations in the Adriatic Islands [22–25]. There is only one study indicating an association with the diet [26], which showed a departure from the traditional MD, and a significant association of high meat, alcohol and fish consumption with MetS. The traditional MD departure was also noted among younger southern Croatia inhabitants [27]. The Croatian Adult Health Survey showed that one-quarter of Croatians had an unhealthy diet, mostly men [28]. The prevalence of MetS in Croatia varies between 25% and 39% [24,29,30], reaching 47% on the isolated Adriatic island of Vis [22]. The main objective of the present study was to investigate the association of MetS and its components with the inflammatory potential of the diet in Croatian working population with sedentary occupations.

Materials and methods

Study population

Overall, 366 workers with sedentary type occupations, out of 547 employees at the oil and gas company from the city of Rijeka on the Croatian northern coast of the Adriatic Sea, participated in the present cross-sectional study. They agreed to participate in a survey named 'Determination of Vitamin D: importance in the prevention of osteoporosis, cardiovascular diseases, type II diabetes, autoimmune diseases and cancer', as organised by the Teaching Institute of Public Health of Primorsko-Goranska County, in December 2014, during their regular health examinations as a part of workplace wellness programme. Based on provided survey results, the participants were referred to see a dietician and health specialist.

Data collection

Trained nutritionists interviewed participants with the questionnaire on sociodemographics, which included information about age, sex, education, physical activity, smoking, leisure lifestyle and particular dietary habits (snacking between meals, adding salt/sugar to meals and beverages). The anthropometric measurements were taken using an electronic scale (BC-544; Tanita, Tokyo, Japan). The waist circumference (WC) measurement of each participant was measured to the nearest 0.1 cm with non-elastic tape. Blood pressure was measured on right arm after 10 min of rest with an automatic monitor (HEM 705 CP; Omron Healthcare Co., Kyoto, Japan). Blood samples were collected in the morning by an experienced nurse after at least 12 h of fasting and were analysed within 1 day of collection. Fasting plasma glucose, triglycerides, total cholesterol and cholesterol linked to high-density lipoproteins (HDL-C) were analysed enzymatically [31–33] with an automatic analyser (model 7600; Hitachi, Tokyo, Japan). The fraction of cholesterol linked to low-density lipoproteins (LDL-C) was calculated using the Friedewald equation [34].

Definition of the metabolic syndrome

The definition of MetS as declared by the International Diabetes Federation Task Force on Epidemiology and Prevention [1] was used for MetS diagnosis, comprising the presence of three or more of the components: WC ≥94 cm for men or ≥80 cm for women; fasting glucose ≥5.6 mmol L^{-1}; HDL-C <1.0 mmol L^{-1} in men and <1.3 mmol L^{-1} in women; triglycerides ≥1.7 mmol L^{-1} and blood pressure ≥130 mmHg for systolic or ≥85 mmHg for diastolic pressure.

Dietary intake assessment

Dietary intakes were assessed with use of validated 97-item food frequency questionnaire for Mediterranean diet-based populations [35], which was adapted and used for diet evaluation of Croatian student [36] and women population [37]. With the assistance of a registered nutritionist, participants noted their usual consumption frequency of offered foods over the last year, considering

seasonal variations, in offered choices from 'never' to 'more than three times a day'. The serving sizes of each offered food were specified as small, medium and large, and were supported with photos. The Croatian food composition database [38] and United States Department of Agriculture (USDA) Database for the Flavonoid Content [39] were used to calculate energy and nutrient intakes. For study purposes, the Mediterranean diet score (MDS) was used to assess the adherence to the MD. The scoring algorithm has been described elsewhere [40]. Good adherence to the MD is defined as a score of 6 or higher, moderate adherence as a score between 4 and 5, and low adherence as a score of 3 or lower.

Dietary Inflammatory Index (DII)® calculation

The inflammatory potential of each participant's diet was calculated using the DII that was designed and developed by Shivappa *et al.* [7]. The dietary data of each participant was first linked to the global means and SD of the food and nutrients intakes from 11 nations [7] to calculate *Z*-scores. These were later converted to a percentile and centred to minimise the 'right skew' by doubling the value and subtracting 1. The provided percentile score of each food parameter was then multiplied by respective inflammatory effect score to provide the food parameter-specific DII score [7]. The overall DII score for each study participant was calculated as a sum of 37 food parameter-specific DII scores of a possible 45 parameters [7]. The calculated 37 food parameters included nine pro-inflammatory components (energy, carbohydrates, protein, total fat, saturated fatty acids, trans fat, cholesterol, iron and vitamin B_{12}) and 28 anti-inflammatory components (monounsaturated fatty acids, polyunsaturated fatty acids, *n*-3 fatty acids, *n*-6 fatty acids, fibre, alcohol, vitamins A, D, E, C and B_6, β-carotene, thiamine, riboflavin, niacin, folic acid, magnesium, selenium, zinc, flavan-3-ol, flavones, flavonols, flavonones, anthocyanidins, caffeine, garlic, onion and pepper). Positive values of the DII score were considered as a pro-inflammatory diet, whereas negative values were considered as an anti-inflammatory diet [7].

Ethical approval

The present study was approved by the Teaching Institute of Public Health of Primorsko-Goranska County for serum vitamin D survey and health and all participants provided their written consent with respect to participation.

Statistical analysis

The data analysis software system STATISTICA, version 13 (TIBCO Software Inc., Palo Alto, CA, USA, 2017) was used for all of the statistical analyses. The Kolmogorov–Smirnov normality test was performed prior to association analysis. Continuous variables are presented as the median and interquartile range, whereas categorical variables are presented as frequencies and percentages. The differences were estimated using Mann–Whitney *U*, Kruskal–Wallis or chi-squared tests depending on the type of variable. The DII scores provided were divided into quartiles: first quartile ($n = 90$; DII = −2.94 to 0.67), second quartile ($n = 90$; DII = 0.86–2.56), third quartile ($n = 93$; DII = 2.58–3.59) and fourth quartile ($n = 93$; DII = 3.65–5.30). Variables associated with MetS were selected to be included in a linear regression model to determine the influence of independent variable: the DII. Univariate logistic regression was performed to specify the odds ratios (ORs) and 95% confidence intervals (CIs) for MetS and its components. The multivariable-adjusted model included sex, age, body mass index (BMI), education, smoking, physical activity and energy intake as potential confounders. $P < 0.05$ (two-tailed) was considered statistically significant.

Results

Among the study participants, there were slightly more women (Table 1), as well as a high proportion of participants who were younger than 40 years, had a university degree, were non-smokers, were moderately physically active, snacked between meals and had a diet that did not adhere to the MD ($P < 0.01$, respectively). The participants were significantly overweight, with elevated WC, total cholesterol and LDL-C levels, although with normal levels of HDL-C, triglycerides and blood pressure ($P < 0.01$, respectively) (Table 2). MetS was present in 24.6% of the participants ($P < 0.01$) and was significantly associated with a higher education, non-smoking, physical activity, snacking between meals, low adherence to MD, being overweight, elevated WC, serum glucose, total cholesterol LDL-C, triglycerides, hypertension and reduced HDL-C ($P < 0.01$, respectively).

The DII ranged from −2.92 to 5.30, with a mean of 2.17. Lower (i.e. more anti-inflammatory) DII values were significantly associated with higher physical activity ($P < 0.01$), not snacking between meals ($P < 0.01$), better adherence to MD ($P < 0.01$) (Table 1), normal BMI ($P = 0.03$) and WC ($P < 0.01$), normal values of total cholesterol ($P = 0.01$), LDL-C ($P = 0.01$), triglycerides ($P < 0.01$) and blood pressure ($P < 0.01$), and not having MetS ($P < 0.01$) (Table 2). The most pro-inflammatory diet (fourth quartile) was statistically associated with women ($P < 0.01$), university degree ($P < 0.01$), moderate physical activity ($P < 0.01$), snacking between meals ($P < 0.01$), elevated WC ($P = 0.01$), elevated triglycerides

Table 1 The Dietary Inflammatory Index® (DII) values and metabolic syndrome (MetS) prevalence according to socio-demographic and lifestyle characteristics of participants

Characteristics	*n* (%)	DII*	*P*-value**	MetS *n* (%)	*P*-value***
Sex					
Men	177 (48.4)	2.39 (1.87)	0.11	54 (60.0)	0.06
Women	189 (51.6)	1.96 (2.03)		36 (40.0)	
Age (years)					
<40 years	234 (63.9)	1.98 (2.10)	0.10	42 (46.7)	0.53
≥40 years	132 (36.1)	2.26 (1.89)		48 (53.3)	
Education level					
University	306 (83.6)	2.09 (2.04)	0.38	75 (83.3)	<0.01***
College	39 (9.8)	2.45 (1.55)		0 (0.0)	
High school	21 (5.7)	2.75 (1.39)		15 (16.7)	
Smoking status					
Non-smoker	183 (50.0)	2.09 (1.84)	0.37	42 (46.7)	0.01***
Former	75 (20.5)	2.34 (2.50)		33 (36.6)	
Current	108 (29.5)	2.18 (1.75)		15 (16.7)	
Physical activity level					
Low	105 (28.7)	3.10 (1.61)	<0.01**	39 (43.3)	<0.01***
Moderate	183 (50.0)	2.02 (1.99)		48 (53.3)	
High	78 (21.3)	1.26 (1.81)		3 (3.4)	
Adds sugar/salt to food/drinks					
Yes	177 (48.4)	2.02 (2.07)	0.27	36 (40.0)	0.06
No	189 (51.6)	2.30 (1.85)		54 (60.0)	
Snacking between meals					
Yes	309 (84.4)	2.56 (1.73)	<0.01**	90 (100.0)	<0.01***
No	57 (15.6)	0.03 (1.78)		0 (0.0)	
Mediterranean diet score					
Low (0–3)	150 (41.0)	3.71 (0.90)	<0.01**	78 (86.6)	<0.01***
Moderate (4–5)	144 (39.3)	1.56 (1.53)		6 (6.7)	
High (6–9)	72 (19.7)	0.15 (1.86)		6 (6.7)	

*The values are reported as the median (interquartile range).

**Continuous variables analysed with the Mann–Whitney or Kruskal–Wallis test; $P < 0.01$.

***Categorical variables analysed by chi-squared analysis; $P < 0.05$.

($P = 0.01$), elevated blood pressure ($P < 0.01$), low HDL-C ($P = 0.01$), having MetS ($P < 0.01$) and lower adherence to MD ($P < 0.01$) (Table 3).

The mean daily intakes of food parameters, used for the calculation of DII, are presented in Table 3. Participants in the first quartile, classified as the most anti-inflammatory group, had the highest MDS score ($P < 0.01$) and consumed almost all of the pro- and anti-inflammatory food components in higher amounts compared to the other participants distributed in the other quartiles, except for trans-fat and caffeine, which were consumed in higher amounts by third and fourth quartile participants.

As shown the Table 4, the results of the odds ratio of MetS and its components were evaluated for a one-unit increase in the DII because the majority of participants (85.2%) had a diet with pro-inflammatory potential (DII higher than 0) and some of them grouped in the first quartile (the most anti-inflammatory diet). Multivariable logistic regression analysis showed a statistically positive association for a one-unit increase in the DII and MetS prevalence (OR = 2.31; 95% CI = 1.61–3.31; $P < 0.01$) and hypertension (OR = 1.28; 95% CI = 1.01–1.64; $P = 0.04$).

Discussion

The present study showed a MetS prevalence of 25%, in accordance with previous Croatian population MetS studies [22–26,29,30]. MetS associations were in line with Croatian studies [22–24,26,29] for smoking, physical activity, being overweight, hyperglycaemia, hyperlipidaemia, hypercholesterolemia and hypertension, despite those studies mostly having been conducted among subjects older than 40 years whereas our participant were mostly younger than 40 years. We noted a higher prevalence of MetS among physically active participants, which can be explained as an attempt by the participants with diagnosed MetS or a MetS component to overcome any adverse effects by being more physically active. In comparison with studies dealing with association of MetS and DII [10,11,13–18], MetS prevalence was similar to a Korean study [15], higher than a Brazilian

Table 2 The Dietary Inflammatory Index® (DII) and metabolic syndrome (MetS) prevalence according to anthropometric and cardiovascular characteristics of participants

Characteristics	*n* (%)	DII†	*P*-value*	MetS *n* (%)	*P*-value**
Body mass index					
Normal	165 (45.1)	1.85 (2.08)	0.03*	15 (16.7)	<0.01**
Overweight	189 (51.6)	2.45 (1.88)		63 (70.0)	
Obese	12 (3.3)	2.05 (0.80)		12 (13.3)	
Waist circumference					
Normal	138 (37.7)	1.91 (2.00)	<0.01*	21 (23.3)	<0.01**
Elevated	228 (62.3)	2.82 (1.53)		69 (76.7)	
Serum glucose					
Normal	174 (47.5)	2.05 (2.01)	0.52	0 (0.0)	<0.01**
Elevated	192 (52.5)	2.27 (1.91)		90 (100.0)	
Total cholesterol					
Normal	117 (32.0)	1.61 (1.89)	<0.01*	9 (10.0)	<0.01**
Elevated	249 (68.0)	2.43 (1.94)		81 (90.0)	
High-density lipoprotein-cholesterol					
Normal	351 (95.9)	2.04 (1.99)	0.35	87 (96.7)	<0.01**
Reduced	15 (4.1)	2.17 (0.99)		3 (3.3)	
Low-density lipoprotein-cholesterol					
Normal	138 (37.7)	1.75 (1.79)	0.01*	15 (16.7)	<0.01**
Elevated	228 (62.3)	2.42 (2.02)		75 (83.3)	
Triglycerides					
Normal	270 (73.8)	1.94 (1.93)	<0.01*	36 (40.0)	<0.01**
Elevated	96 (26.2)	2.80 (1.92)		54 (60.0)	
Blood pressure					
Normal	243 (66.4)	1.89 (1.99)	<0.01*	9 (10.0)	<0.01**
Hypertension	123 (33.6)	2.71 (1.80)		81 (90.0)	
Metabolic syndrome					
No	276 (75.4)	1.80 (1.97)	<0.01*	0 (0.0)	<0.01**
Yes	90 (24.6)	3.28 (1.45)		90 (100.0)	

†The values are reported as the median (interquartile range).

*Continuous variables analysed with the Mann–Whitney or Kruskal–Wallis test; $P < 0.01$.

**Categorical variables analysed by chi-squared analysis; $P < 0.05$.

study [17], and lower than Luxemburg [9], Poland [13] and Lebanon [14] studies. Our study found a significant association of MetS with DII, which is comparable with the French prospective study [11], the cross-sectional Korean study [15] and Irish [18] studies, as well as with a Columbian cohort study on overweight sedentary subjects [41], although the researchers used MetScore for diagnosing MetS, as well as different statistical analyses. Indeed, the present study revealed that those who had the most pro-inflammatory diet had a two-fold higher chance to have MetS, which is higher than in the previously mentioned studies [11,15,18]. A possible explanation of this association could be that high proportion of our participants had a diet with pro-inflammatory potential and one-third of them had MetS. Although some MetS-DII studies [10,11,13,17] did not find a significant association of Mets with DII, the associations were found for MetS components, lower HDL-C levels [9], glucose intolerance [10] and greater blood pressure [13,16,21], which is similar to our results for hypertension. Most of our participants were younger than 40 years with a mostly pro-inflammatory potential of the diet, which is similar to the Luxembourg [9] and Brazilian [17] studies.

Our study showed that low adherence to the MD was associated with a significantly higher prevalence of MetS, and confirmed a diminishing adherence to the traditional MD among Croatians [26,27]. The significantly higher consumption of almost all pro-inflammatory food components, except trans-fat, by participants in the first quartile (most anti-inflammatory) is probably because 85.2% of study participants had a DII higher than 0 (i.e. indicating a pro-inflammatory diet). The consumption of pro-inflammatory food components, mostly originated from animal-origin food with an abundance of proteins, saturated fats and cholesterol. Those results are in line with the prevously mentioned Croatian studies [26,27]. However, first quartile participants also consumed significantly higher amounts of anti-inflammatory food components compared to the others.

Recent meta-analyses studies have observed a considerable association between the DII and the risk for CVD

Table 3 Characteristics and food parameters daily intake of participants according to Dietary Inflammatory Index® (DII) quartiles

Characteristics	DII quartiles†				*P*-value*
	First (*n* = 90)	Second (*n* = 90)	Third (*n* = 93)	Fourth (*n* = 93)	
Men	30 (33.3)	51 (56.7)	60 (64.5)	36 (38.7)	<0.01*
Age <40 years	57 (63.3)	57 (63.3)	60 (64.5)	69 (74.2)	0.33
Education level					
University	81 (90.0)	69 (76.7)	72 (77.4)	84 (90.3)	<0.01*
College	3 (3.3)	21 (23.3)	12 (12.9)	3 (3.2)	
High school	6 (6.7)	0 (0.0)	9 (9.7)	6 (6.5)	
Smoking status					
Non-smoker	45 (50.0)	48 (53.3)	45 (48.4)	45 (48.4)	0.12
Former	18 (20.0)	9 (10.01)	24 (25.8)	24 (25.8)	
Current	27 (30.0)	33 (36.7)	24 (25.8)	24 (25.8)	
Physical activity level					
Low	12 (13.3)	15 (16.7)	45 (48.4)	33 (35.5)	<0.01*
Moderate	45 (50.0)	45 (50.0)	42 (45.2)	51 (54.8)	
High	33 (36.7)	30 (33.3)	6 (6.4)	9 (9.7)	
Adds sugar/salt to food/drinks	51 (56.7)	42 (46.7)	39 (41.9)	45 (48.4)	0.25
Snacking between meals	48 (53.3)	84 (93.3)	84 (90.3)	93 (100.0)	<0.01*
Elevated waist circumference	18 (20.0)	18 (20.0)	33 (35.5)	33 (35.5)	0.01*
Elevated fasting glucose	45 (50.0)	42 (46.7)	60 (64.5)	45 (48.4)	0.06
Low high-density lipoprotein-cholesterol	0 (0.0)	6 (6.7)	9 (9.7)	0 (0.0)	0.01*
Elevated triglycerides	18 (20.0)	9 (10.0)	36 (38.7)	33 (35.5)	0.01*
Elevated blood pressure	27 (30.0)	9 (10.0)	54 (58.1)	33 (35.5)	<0.01*
Metabolic syndrome	9 (10.0)	9 (10.0)	36 (38.7)	36 (38.7)	<0.01*
Mediterranean diet score	6.00 (3.00)	5.00 (4.00)	3.00 (5.00)	2.00 (3.00)	<0.01*
Energy (MJ)	10.18 (6.82)	9.28 (5.61)	8.47 (7.85)	7.27 (5.69)	0.01*
Proteins (g)	104.07 (84.44)	91.74 (59.38)	87.12 (78.17)	64.91 (72.88)	0.01*
Total fat (g)	100.97 (71.68)	86.79 (63.00)	79.99 (83.82)	65.64 (59.19)	0.01*
Saturated fat (g)	38.24 (46.53)	37.81 (30.81)	34.03 (57.03)	30.34 (27.91)	<0.01*
MUFA (g)	49.40 (60.87)	36.64 (27.44)	30.45 (33.22)	26.90 (21.83)	0.01*
PUFA (g)	17.98 (20.51)	12.58 (14.95)	10.50 (12.99)	8.29 (10.39)	0.01*
Omega-3 (g)	1.20 (0.59)	1.09 (0.24)	0.89 (0.27)	0.94 (0.26)	<0.01*
Omega-6 (g)	11.60 (4.58)	11.60 (3.58)	10.01 (3.15)	10.48 (4.76)	0.03*
Trans fat (g)	1.65 (1.64)	1.85 (2.20)	1.84 (3.30)	1.86 (2.75)	0.66
Cholesterol (mg)	444.61 (528.18)	431.38 (372.45)	361.41 (505.34)	305.41 (344.89)	<0.01*
Carbohydrates (g)	243.82 (226.35)	206.21 (158.05)	199.32 (198.26)	208.71 (151.77)	0.01*
Fibre (g)	22.71 (17.20)	16.86 (10.85)	12.22 (12.49)	8.43 (11.90)	0.01*
Thiamine (mg)	2.71 (2.24)	1.81 (1.42)	1.61 (2.39)	1.71 (2.24)	0.01*
Riboflavin (mg)	2.88 (2.23)	1.92 (1.54)	1.90 (3.78)	1.76 (2.36)	<0.01*
Niacin (mg)	18.31 (13.77)	14.25 (4.32)	14.23 (4.11)	10.72 (18.17)	0.01*
Pyridoxine (mg)	1.45 (0.69)	1.33 (1.23)	1.24 (1.66)	1.18 (0.47)	0.01*
Folic acid (mg)	287.55 (277.87)	201.24 (109.40)	150.84 (162.52)	126.63 (40.43)	0.01*
Vitamin B_{12} (μg)	2.04 (1.28)	1.81 (1.43)	1.79 (1.85)	1.83 (1.17)	<0.01*
Vitamin A (mg)	455.14 (332.14)	378.72 (351.04)	353.74 (347.99)	313.60 (323.64)	<0.01*
Vitamin C (mg)	126.45 (104.78)	84.88 (134.87)	64.35 (123.09)	39.22 (57.87)	0.01*
Vitamin D (μg)	9.90 (21.21)	8.69 (12.12)	7.30 (10.54)	5.66 (12.08)	<0.01*
Vitamin E (mg)	6.69 (4.29)	5.32 (5.40)	5.31 (3.12)	4.71 (3.57)	0.01*
Magnesium (mg)	304.31 (132.44)	256.35 (180.73)	251.97 (175.31)	204.66 (134.11)	0.01*
Iron (mg)	15.63 (13.11)	12.14 (13.86)	11.28 (12.79)	9.05 (12.72)	0.01*
Zinc (mg)	14.96 (12.89)	12.58 (8.72)	11.80 (15.36)	9.12 (11.96)	0.01*
Selenium (μg)	51.33 (95.09)	48.67 (47.01)	33.07 (39.45)	26.99 (62.78)	0.01*
Alcohol (g)	4.29 (15.86)	4.29 (14.14)	5.14 (11.57)	1.00 (4.70)	<0.01*
Caffeine (g)	15.14 (31.80)	15.01 (30.16)	21.20 (31.80)	21.20 (31.80)	0.01*
Flavan-3-ol (mg)	30.14 (37.02)	24.36 (32.47)	16.19 (28.49)	7.40 (30.09)	0.01*
Flavones (mg)	1.92 (1.68)	1.46 (2.12)	1.01 (2.02)	0.92 (1.47)	0.01*
Flavonols (mg)	18.91 (19.40)	15.40 (12.34)	10.48 (12.60)	9.23 (13.93)	0.01*

Table 3 Continued

Characteristics	DII quartiles†				*P*-value*
	First (*n* = 90)	Second (*n* = 90)	Third (*n* = 93)	Fourth (*n* = 93)	
Flavonones (mg)	206.56 (418.38)	124.58 (269.37)	110.50 (300.93)	14.60 (196.21)	0.01*
Anthocyanidins (mg)	12.85 (30.65)	5.17 (22.36)	1.30 (21.83)	0.46 (14.18)	0.01*

†The values are reported as the median (interquartile range) or *n* (%).
*Continuous variables analysed with the Kruskal–Wallis test; categorical variables analysed by chi-squared analysis $P < 0.05$.
MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids.

Table 4 Crude and adjusted association of Dietary Inflammatory Index® (DII) with metabolic syndrome (MetS) and its components

MetS/ components	Crude OR (95% CI)	*P*-value*	Adjusted† OR (95% CI)	*P*-value*
Metabolic syndrome				
DII (unit)	1.97 (1.54–2.51)	<0.01*	2.31 (1.61–3.31)	<0.01*
Central obesity				
DII (unit)	1.37 (1.11–1.69)	0.01*	1.32 (0.94–1.85)	0.11
Hyperglycaemia				
DII (unit)	1.05 (0.88–1.26)	0.58	0.85 (0.66–1.10)	0.22
Hypertriglyceridaemia				
DII (unit)	1.50 (1.20–1.86)	0.01*	1.29 (0.98–1.69)	0.07*
Hypertension				
DII (unit)	1.34 (1.10–1.64)	0.01*	1.28 (1.01–1.64)	0.04*
Low high-density lipoprotein-cholesterol				
DII (unit)	1.07 (0.67–1.70)	0.77	1.27 (0.67–2.43)	0.47

†Adjusted for sex, age, educational level, smoking, physical activity, body mass index and energy intake.
*$P < 0.01$.
CI, confidence interval; OR, odds ratio.

and all types of mortality [19,42]. If our participants continue with pro-inflammatory dietary habits, they can put themselves at risk for CVD and all-cause mortality. Former or current smokers had a pro-inflammatory potential of their diet, which might represent a possible risk for developing oral, lung and pharyngeal cancer [43]. Smoking is connected with a higher MetS risk, although consequent weight-gain after smoking cessation, if unhealthy dietary habits continue, may also increase the risk of MetS [3]. However, current smoking appears to have a protective effect on MetS among 3245 Croatian participants [29] and our current smokers had significantly the lowest prevalence of MetS. A significant proportion of participants snacked between meals, which all had MetS and were mainly grouped in more pro-inflammatory diet quartiles. The 'unhealthy snacking pattern' was independently associated with increased MetS among Spanish young participants [44], and our similar study results present a strong need for public health diet education and/or intervention programmes aimed at younger generations, toward reviving traditional MD. The present study revealed that adding sugar/salt to food was not connected with MetS, nor to a pro-inflammatory diet, which may be because participants use them only in moderation.

Strengths and limitations

The present study should be regarded with some limitations, such as the use of a self-reported food frequency questionnaire and consequent under- or over-reporting by participants. Still, possible mistakes are minimal because questionnaire fulfilling was guided and monitored by skilled nutritionists. The cross-sectional study nature prevents us from making any conclusions regarding causality and temporal outcome of the observed significant association of dietary inflammatory potential and MetS. In addition, some of the studied participants diagnosed with some aspects of MetS may have made some dietary changes. Therefore, their diet may appear to be healthier than that of those without MetS. Consequently, the change in diet could create an artefact of more pro-inflammatory DII scores not being associated, or even being protective, in some cases of MetS or its components, although such changes have not been demonstrated in the present study. In Croatia, general practitioners conduct nutrition counselling. However, only 18.7% of Croatian general practitioners always conduct nutrition counselling with their patients, regardless of their individual health risks, and 81.6% of them mentioned a lack of time as being the most significant barrier for nutrition counselling [45]. These findings could indicate that MetS patients may not receiving adequate nutrition counselling, which therefore could have influenced the results of the present study.

The rather small study sample, consisting of workers from one company and localised to one part of Croatia, might give inadequate results with respect to the association of DII and MetS in Croatia. The DII results showed a significantly small proportion of participants with an anti-inflammatory diet, which could be a result of the limited presentation of DII components with anti-inflammatory potential, such as ginger, turmeric, rosemary, thyme/oregano and green/black tea, in the food frequency questionnaire. Croatia lacks consumption data of these food items at a national or regional level. The original

research (i.e. from which the present study results) was primarily designed with different monitoring objectives and had limited resources that did not enable researchers to include inflammatory biomarkers possibly revealing a better diet–disease association. Another possible limitation is the use of USDA Database for the Flavonoid Content, which only contains data on flavonoids expressed as aglycones.

However, the present study has its strengths. This is the first Croatian study reporting data on the inflammation potential of the diet among Croatians, as assessed with 37 nutrients used for scoring the DII, and presenting a significant association of pro-inflammatory diet to MetS. The study results are significant with respect to emphasising the worrying diet–disease situation among the younger Croatian population. Although the study findings may be of public health significance as a result of using anti-inflammatory dietary approaches to protect cardiometabolic health, there is the need for further examinations including endocrine and inflammatory biomarkers to clarify the DII and MetS association among Croatians. Croatia has been classified as a country with a high risk for CVD [46] and CVD mortality rates are almost twice as high as the European Union average, which points to shortcomings in healthcare delivery and public health interventions, according to European Comity Country Health Profile 2017 [47]. By promoting and adopting a more anti-inflammatory diet, which might comprise reviving the MD heritage, Croatians may improve their cardio-metabolic profile and attenuate the risk of CVD and MetS. MD has been proven as a good dietary intervention for MetS prevention and management [48].

Conclusions

The present study demonstrates a significant association of DII with MetS and hypertension. There was a significant proportion of participants with a pro-inflammatory diet, mostly younger than 40 years, which represents a risk for CVD development in later life. Further longitudinal studies in different parts of Croatia, including inflammation biomarkers, are needed for a more defined view of the inflammatory potential of the diet and its association with various inflammatory-based health conditions. The reported results indicate the need for the development of anti-inflammatory dietary interventions for population health protection.

Transparency declaration

The lead author affirms that this manuscript is an honest, accurate and transparent account of the study being reported. The reporting of this work is compliant with STROBE guidelines. The lead author affirms that no important aspects of the study have been omitted and that any discrepancies from the study as planned have been explained.

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Conflict of interests, source of funding and authorship

The authors declare that they have no conflicts of interest.

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GKJ, SPŽ, SKM and IMŠ contributed equally to the conception and design of the study and data interpretation. GKJ and SPŽ contributed to the generation, collection, assembly, analysis and/or interpretation of data. IŠ contributed to data analysis and interpretation. GKJ drafted the manuscript. GKJ, SPŽ, SKM, IMŠ and IŠ critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript submitted for publication.

References

1. Alberti KG, Eckel RH, Grundy SM *et al.* (2009) Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation* **120**, 1640–1645.
2. Ahluwalia N, Andreeva VA, Kesse-Guyot E *et al.* (2013) Dietary patterns, inflammation and the metabolic syndrome. *Diabetes Metab* **39**, 99–110.
3. Pérez-Martínez P, Mikhailidis DP, Athyros VG *et al.* (2017) Lifestyle recommendations for the prevention and management of metabolic syndrome: an international panel recommendation. *Nutr Rev* **75**, 307–326.
4. Lopez-Candales A, Hernández Burgos PM, Hernandez-Suarez DF *et al.* (2017) Linking chronic inflammation with cardiovascular disease: from normal aging to the metabolic syndrome. *J Nat Sci* **3**, e341.
5. Salas-Salvadó J, Garcia-Arellano A, Estruch R *et al.* (2008) Components of the Mediterranean-type food pattern and serum inflammatory markers among patients at high risk for cardiovascular disease. *Eur J Clin Nutr* **62**, 651–659.

6. Medina-Remón A, Casas R, Tressserra-Rimbau A *et al.* (2017) Polyphenol intake from a Mediterranean diet decreases inflammatory biomarkers related to atherosclerosis: a sub-study of the PREDIMED trial. *Br J Clin Pharmacol* **83**, 114–128.
7. Shivappa N, Steck SE, Hurley TG *et al.* (2014) Designing and developing a literature-derived, population-based dietary inflammatory index. *Public Health Nutr* **17**, 1689–1696.
8. Shivappa N, Steck SE, Hurley TG *et al.* (2014) A population-based dietary inflammatory index predicts levels of C-reactive protein in the Seasonal Variation of Blood Cholesterol Study (SEASONS). *Public Health Nutr* **17**, 1825–1833.
9. Alkerwi A, Shivappa N, Crichton G *et al.* (2014) No significant independent relationships with cardiometabolic biomarkers were detected in the Observation of Cardiovascular Risk Factors in Luxembourg study population. *Nutr Res* **34**, 1058–1065.
10. Wirth MD, Burch J, Shivappa N *et al.* (2014) Association of a dietary inflammatory index with inflammatory indices and metabolic syndrome among police officers. *J Occup Environ Med* **56**, 986–989.
11. Neufcourt L, Assmann KE, Fezeu LK *et al.* (2015) Prospective association between the dietary inflammatory index and metabolic syndrome: findings from the SU.VI.MAX study. *Nutr Metab Cardiovasc Dis* **25**, 988–996.
12. Pimenta AM, Toledo E, Rodriguez-Diez MC *et al.* (2015) Dietary indexes, food patterns and incidence of metabolic syndrome in a Mediterranean cohort: the SUN project. *Clin Nutr* **34**, 508–514.
13. Sokol A, Wirth MD, Manczuk M *et al.* (2016) Association between the dietary inflammatory index, waist-to-hip ratio and metabolic syndrome. *Nutr Res* **36**, 1298–1303.
14. Naja F, Shivappa N, Nasreddine L *et al.* (2017) Role of inflammation in the association between the western dietary pattern and metabolic syndrome among Lebanese adults. *Int J Food Sci Nutr* **68**, 997–1004.
15. Kim HY, Lee J & Kim J (2018) Association between dietary inflammatory index and metabolic syndrome in the general korean population. *Nutrients* **10**, 648.
16. Ren Z, Zhao A, Wang Y *et al.* (2018) Association between dietary inflammatory index, C-reactive protein and metabolic syndrome: a cross-sectional study. *Nutrients* **10**, 831.
17. Carvalho CA, Silva AAM, Assunção MCF *et al.* (2018) The dietary inflammatory index and insulin resistance or metabolic syndrome in young adults. *Nutrition* **58**, 187–193.
18. Phillips CM, Shivappa N, Hébert JR *et al.* (2018) Dietary inflammatory index and biomarkers of lipoprotein metabolism, inflammation and glucose homeostasis in adults. *Nutrients* **10**, 1033.
19. Namazi N, Larijani B & Azadbakht L (2018) Dietary inflammatory index and its association with the risk of cardiovascular diseases, metabolic syndrome, and mortality: a systematic review and meta-analysis. *Horm Metab Res* **50**, 345–358.
20. Ruiz-Canela M, Zazpe I, Shivappa N *et al.* (2015) Dietary inflammatory index and anthropometric measures of obesity in a population sample at high cardiovascular risk from the PREDIMED (PREvención con DIeta MEDiterránea) trial. *Br J Nutr* **113**, 984–995.
21. Vissers LET, Waller M, van der Schouw YT *et al.* (2017) A pro-inflammatory diet is associated with increased risk of developing hypertension among middle-aged women. *Nutr Metab Cardiovasc Dis* **27**, 564–570.
22. Kolcić I, Vorko-Jović A, Salzer B *et al.* (2006) Metabolic syndrome in a metapopulation of Croatian island isolates. *Croat Med J* **47**, 585–592.
23. Deka R, Durakovic Z, Niu W *et al.* (2012) Prevalence of metabolic syndrome and related metabolic traits in an island population of the Adriatic. *Ann Hum Biol* **39**, 46–53.
24. Deka R, Narancić NS, Xip H *et al.* (2008) Metabolic syndrome in an island population of the eastern Adriatic coast of Croatia. *Coll Antropol* **32**, 85–91.
25. Karmelić I, Lovrić J, Božina T *et al.* (2017) Is there any association of apolipoprotein E gene polymorphisms with metabolic syndrome in a young population of Croatian origin? *Ann Hum Biol* **44**, 287–294.
26. Sahay RD, Couch SC, Missoni S *et al.* (2013) Dietary patterns in adults from an Adriatic Island of Croatia and their associations with metabolic syndrome and its components. *Coll Antropol* **37**, 335–342.
27. Kolčić I, Relja A, Gelemanović A *et al.* (2016) Mediterranean diet in the southern Croatia – does it still exist? *Croat Med J* **31**, 415–424.
28. Jelinić JD, Pucarin-Cvetković J, Nola IA *et al.* (2009) Regional differences in dietary habits of adult Croatian population. *Coll Antropol* **33** (Suppl 1), 31–34.
29. Ivezić-Lalić D, Bergman Marković B, Kranjčević K *et al.* (2013) Diversity of metabolic syndrome criteria in association with cardiovascular diseases–a family medicine-based investigation. *Med Sci Monit* **19**, 571–578.
30. Vuletić S, Kern J, Ivanković D *et al.* (2007) Metabolic syndrome in the Croatian population – the multiple cardiovascular risks. *Acta Med Croatica* **61**, 239–243 [in Croatian].
31. Trinder P (1969) Determination of glucose in blood using glucose oxidase with an alternative oxygen receptor. *Ann Clin Biochem* **6**, 24–27.
32. Siedel J, Hägele EO, Ziegenhorn J *et al.* (1983) Reagent for the enzymatic determination of serum total cholesterol with improved lipolytic efficiency. *Clin Chem* **29**, 1075–1080.
33. Fossati P & Prencipe L (1982) Serum triglycerides determined colorimetrically with an enzyme that produces hydrogen peroxide. *Clin Chem* **28**, 2077–2080.

34. Friedewald WT, Levy RI & Fredrickson DS (1972) Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem* **18**, 499–502.
35. Martin-Moreno JM, Boyle P, Gorgojo L *et al.* (1993) Development and validation of a food frequency questionnaire in Spain. *Int J Epidemiol* **22**, 512–519.
36. Kresić G, Kendel Jovanović G, Pavicić Zezelj S *et al.* (2009) The effect of nutrition knowledge on dietary intake among Croatian university students. *Coll Antropol* **33**, 1047–1056.
37. Jovanović GK, Zezelj SP, Malatestinić D *et al.* (2010) Diet quality of middle age and older women from Primorsko-Goranska County evaluated by healthy eating index and association with body mass index. *Coll Antropol* **34**(Suppl 2), 155–160.
38. Kaić Rak A & Antonić K (1990) Tables of Chemical Composition of Food and Drinks. Zagreb: Institute for Public Health.
39. Bhagwat S & Haytowitz DB (2015) USDA Database for the Flavonoid Content of Selected Foods, Release 3.2. Beltsville, MD: US Department of Agriculture, Agricultural Research Service.
40. Trichopoulou A, Kouris-Blazos A, Wahlqvist ML *et al.* (1995) Diet and overall survival in elderly people. *BMJ* **311**, 1457–1460.
41. Camargo-Ramos CM, Correa-Bautista JE, Correa-Rodríguez M *et al.* (2017) Dietary inflammatory index and cardiometabolic risk parameters in overweight and sedentary subjects. *Int J Environ Res Public Health* **14**, 1104.
42. Shivappa N, Godos J, Hébert JR *et al.* (2018) Dietary inflammatory index and cardiovascular risk and mortality-a meta-analysis. *Nutrients* **10**, 200.
43. Shivappa N, Hébert JR, Rosato V *et al.* (2017) Inflammatory potential of diet and risk of oral and pharyngeal cancer in a large case-control study from Italy. *Int J Cancer* **141**, 471–479.
44. Pimenta AM, Bes-Rastrollo M, Gea A *et al.* (2016) Snacking between main meals is associated with a higher risk of metabolic syndrome in a Mediterranean cohort: the SUN Project (Seguimiento Universidad de Navarra). *Public Health Nutr* **19**, 658–666.
45. Dumic A, Miskulin I, Matic Licanin M *et al.* (2017) Nutrition counselling practices among general practitioners in Croatia. *Int J Environ Res Public Health* **14**, 1499.
46. Piepoli MF, Hoes AW, Agewall S *et al.* (2016) 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* **37**, 2315–2381.
47. OECD/European Observatory on Health Systems and Policies (2017) Croatia: Country Health Profile 2017, State of Health in the EU, OECD Publishing, Paris/European Observatory on Health Systems and Policies, Brussels. Available at: http://sci-hub.tw/10.1787/9789264283312-en (accessed on 28 May 2018).
48. Castro-Barquero S, Ruiz-León AM, Sadurní M *et al.* (2017) Dietary strategies for metabolic syndrome: a review. *J Obes Ther* **1**.

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INFLAMMATORY DISORDERS

Dietary inflammatory index and mortality: a cohort longitudinal study in a Mediterranean area

N. Veronese[1,2] A. M. Cisternino,[1] N. Shivappa,[3,4,5] J. R. Hebert,[3,4,5] M. Notarnicola,[2] R. Reddavide,[1] R. Inguaggiato,[1] V. Guerra,[6] A. Logroscino,[7] O. Rotolo,[1] M. Chiloiro,[8] G. Leandro,[9] G. De Leonardis,[1,2] V. Tutino,[2] G. Misciagna,[10] L. Fontana,[11,12] M. G. Caruso,[1,2] & The MICOL group*

[1]Ambulatory of Clinical Nutrition, National Institute of Gastroenterology 'S. De Bellis' Research Hospital, Bari, Italy
[2]Laboratory of Nutritional Biochemistry, National Institute of Gastroenterology 'S. De Bellis' Research Hospital, Bari, Italy
[3]Cancer Prevention and Control Program, Arnold School of Public Health, University of South Carolina, Columbia, SC, USA
[4]Department of Epidemiology and Biostatistics, Arnold School of Public Health, University of South Carolina, Columbia, SC, USA
[5]Connecting Health Innovations LLC, Columbia, SC, USA
[6]Clinical Trial Unit, National Institute of Gastroenterology 'S. De Bellis' Research Hospital, Bari, Italy
[7]Thoracic Medical Oncology, I.R.C.C.S. 'Giovanni Paolo II', Bari, Italy
[8]Radiology Unit, Hospital San Giacomo, Bari, Italy
[9]Unit of Gastroenterology, National Institute of Gastroenterology 'S. De Bellis' Research Hospital, Bari, Italy
[10]Scientific and Ethical Committee, University Hospital Policlinico, Bari, Italy
[11]Central Clinical School and Charles Perkins Centre, University of Sydney, Sydney, NSW, Australia
[12]Department of Clinical and Experimental Sciences, Brescia University Medical School, Brescia, Italy

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Correspondence
N. Veronese, National Institute of Gastroenterology 'S. De Bellis' Research Hospital, Castellana Grotte, Bari, Italy. Via Turi 27, 70013 Castellana (Bari), Italy.
Tel.: +39 080 4994669
Emails: nicola.veronese@irccsdebellis.it; ilmannato@gmail.com

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*The MICOL group members are listed in the Appendix

Abstract

Background: Higher Dietary Inflammatory Index (DII®) scores are associated with increased morbidity and mortality. However, little is known about the effects of DII on mortality in Mediterranean countries. Therefore, in the present study, we aimed to investigate the potential association between DII scores and overall, cancer and cardiovascular disease (CVD) mortality in people living in a Mediterranean area.
Methods: DII scores were calculated using a validated food-frequency questionnaire. DII scores were then categorised into tertiles. Mortality was ascertained via death certificates. The association between DII scores with overall and cause-specific mortality was assessed via a multivariable Cox's regression analysis and reported as hazard ratios (HRs) with their 95% confidence intervals (CIs).
Results: The study included 1565 participants (mean age 65.5 years; females 44.7%). After a median follow-up of 12 years (2005–2017), 366 (23.4%) participants died. After adjusting for 17 potential confounders, people with higher DII scores had an increased risk of death compared to those in the lowest (most anti-inflammatory) tertile (HR = 1.38; 95% CI = 1.04–1.82 for the second tertile; HR = 1.38; 95% CI = 1.03–1.86 for the third tertile). Each 1 SD increase in DII score increased the risk of death by 13%. No association was found between DII scores and cancer or CVD death when considered separately.
Conclusions: Higher DII scores were associated with a significantly higher mortality risk, whereas the association with cause-specific mortality was less clear. These findings highlight the potential importance of diet in modulating inflammation and preventing death.

Introduction

Chronic systemic inflammation has been proposed as a pivotal factor in the development and progression of several non-communicable diseases, including cardiovascular disease (CVD), cancer, type 2 diabetes and dementia [1]. Accumulating data have shown that diet is one of the most important contributors to chronic systemic inflammation.

Accumulating data have shown that an unhealthy diet is one of the most important contributors to chronic systemic inflammation [2].

In the updated version of the Dietary Inflammatory Index (DII®) [2], 1943 articles were reviewed and scored. Forty-five food parameters, including foods, nutrients and other bioactive compounds, were identified based on their inflammatory effect on six specific inflammatory markers, including C-reactive protein (CRP), interleukin (IL)-1β, IL-4, IL-6, IL-10 and tumour necrosis factor-α [3–8]. The DII has been shown to be a valid tool for predicting levels of inflammatory markers, including IL-6 and CRP [3,9–11]. Thus, it provides a useful and readily comparable means for estimating the inflammatory nature of an individual's diet based on the pro- and anti-inflammatory power of the overall diet, taking into consideration both macro and micronutrients in any population [12].

Several studies have reported an association between an increasing DII score and levels of biochemical inflammatory parameters [3,13], leading to the hypothesis that a diet with high levels of pro-inflammatory components might be related to an increased risk for some medical conditions such as CVD [14,15], cancer [16], diabetes [17] and bone fractures [18]. All of these medical conditions are traditionally associated with an increased risk of mortality, suggesting that higher DII scores could be associated with a higher overall mortality risk [19,20].

In a large meta-analysis [14], including six prospective studies investigating the potential association between DII scores and mortality, the consumption of a more pro-inflammatory diet was associated with a higher risk of all-cause, CVD and cancer mortality. However, the studies included in this meta-analysis were mainly derived from populations residing primarily outside of the Mediterranean region [14]. Given the popularity of the Mediterranean diet, findings concerning the possible association between higher DII scores and all-cause and cause-specific mortality could be of interest, especially because it was recently noted that these countries are eating less healthy diets than previously reported [21]. Additionally, to the best of our knowledge, only one study has been published based on a Mediterranean population [22]. Additionally, the DII has been validated with low-grade inflammation in another Mediterranean population [23].

Given this background, we aimed to investigate the potential association between DII and mortality (overall and cause-specific forms) in a sample of older people living in a Mediterranean area.

Materials and methods

Participants

The study included women and men randomly sampled from the electoral rolls of the population of Castellana Grotte, a town in Southern Italy (Apulia region) between 2005 and 2006. Among 1942 individuals initially contacted, 1708 (87.9%) participated to the baseline survey [MICOL (Multicentrica Italiana COLeleitiasi) III]. This research was approved by the Institutional Review Board (Ethical Committee) of IRCCS De Bellis and written informed consent was obtained from each participant before entering the study.

Exposure: dietary inflammatory index

Dietary intake was assessed using a validated tool, comprising the Block Brief 2000 food frequency questionnaire (FFQ) during the baseline visit that was adapted for use in this population [24].

Seventy items were assessed to determine an individual's typical food and beverage consumption over the past year. The frequency of consumption was reported at nine levels of intake from 'never' to 'every day'. The data for DII calculation were extracted using the Food Composition Database for Epidemiological Studies in Italy [25].

Details describing the development of the DII are provided elsewhere [2]. Individual scores were computed for each food parameter for each participant based on the FFQ.

The FFQ in the present study provided data on 26 food parameters (of the 45 possible) from which we calculated energy-adjusted DII (E-DII) scores based on intake standardised to 4184 kJ (1000 kcal) of energy [26]. The 26 food parameters available for DII calculation in this study were vitamin B_{12}, vitamin B_6, β-carotene, carbohydrate, cholesterol, fat, fibre, folic acid, iron, magnesium, monounsaturated fat acids, niacin, protein, polyunsaturated fatty acids, omega 3 and 6, riboflavin, saturated fat acids, selenium, thiamin, vitamin A, vitamin C, vitamin E, vitamin D, zinc and niacin.

To create a means for comparing diets in different populations, a regionally representative world database representing diet surveys from 11 countries was used as a comparative standard for all of the parameters (i.e. foods, nutrients, and other food components) that comprise the DII. To compute the E-DII, we used an

energy-standardised (to 1000 kcal) version of the comparative database. Briefly, a standard mean for each parameter from the energy-standardised representative world database was subtracted from the individual's reported intake and divided by the SD of the representative world database to generate *Z*-scores. These *Z*-scores were converted to proportions (thus minimising effects of outliers/right-skewing). These values were then doubled and 1 was subtracted to achieve symmetrical distribution with values centered on 0. The resulting value was then multiplied by the corresponding inflammatory score for each food parameter and summed across all food parameters, obtaining the overall DII score.

Outcome: vital status

The primary outcome of interest of the present study was all-cause mortality. In the MICOL III, mortality was adjudicated via death certificates, manually revised by a trained researcher. Examination of the death certificates was carried out up to 31 December 2017. Cardiovascular death was assigned based on ICD-10 (International Statistical Classification of Diseases) codes from I00 to I99 and cancer-related death was associated with codes from C00 to C97.

Other measurements

The survey visit consisted of the administration of a standardised questionnaire, including the FFQ, anthropometric measurements, a blood sample for biochemical tests and an ultrasonographic examination.

A scale indicating the degree of adherence to the traditional Mediterranean diet (aMED) was constructed using the indications given by Trichopoulou *et al.* [27], which was revised to include fish intake. The total Mediterranean diet score ranged from 0 (minimal adherence to the traditional Mediterranean diet) to 9 (maximal adherence).

Depressive symptoms were measured using the Zung Self-Rating Depression Scale, with scores >50 (out of 100) indicating the presence of depressive symptoms [28].

Smoking status was categorised as actual/previous versus never. A trained nurse recorded weight and height. Body mass index (BMI) was then calculated and reported in as weight (kg)/height $(m)^2$. Systolic and diastolic blood pressure also were recorded by a trained nurse. All the subjects underwent a standardised ultrasound examination made by two investigators using a Hitachi H21 Vision® (Hitachi Medical Corporation, Tokyo, Japan). Examination of the visible liver parenchyma was performed with a 3.5-MHz transducer. A scoring system was adopted to obtain a semi-quantitative evaluation of fat in the liver.[29] The fatty liver score ranged from 0 to 6, with higher values indicating higher severity [30].

Finally, self-reported information regarding the presence of diabetes, gastric ulcer, gall stones, hepatic cirrhosis, cancer, acute myocardial infarction were used in the analyses.

Statistical analysis

Data on continuous variables were normally distributed according to the Kolmogorov–Smirnov test. Data were presented as the means (SD) for quantitative measures, and as frequency and percentages for all discrete variables. Levene's test was used to test the homoscedasticity of variances and, if its assumption was violated, Welch's analysis of variance was used. *P*-values were calculated using the Jonckheere–Terpstra test[31] for continuous variables and the Mantel–Haenszel chi-squared test for categorical variables.

To assess the relationship between DII scores and mortality, a Cox's regression analysis was conducted where mortality was defined as the discrete 'outcome', time-to-event was the temporal factor and the DII score was the 'exposure'. The basic model was not adjusted for any confounders. The fully adjusted model included the covariates: age, sex, smoking status, diabetes, gastric ulcer, gallbladder stones, hepatic cirrhosis, cancer, acute myocardial infarction, body mass index, systolic and diastolic blood pressure, presence of depressive symptoms, presence of hepatic steatosis, energy and alcohol intake, and aMED score.

Multicollinearity among covariates was assessed via variance inflation factor (VIF) [32], taking a cut-off of 2 as the criterion for exclusion. No covariates met this criterion, and therefore none of them was excluded for this reason. The VIF between DII and aMED was 1.46, taking overall mortality as outcome. Adjusted hazard ratios (HR) and 95% confidence intervals (CI) were calculated to estimate the strength of the associations between DII scores (reported in tertiles) and mortality. We finally modelled DII as continuous variable, reporting the association between increase in 1 SD as exposure variable. Similar analyses were run taking CVD death and cancer-specific death as outcome.

Several sensitivity analyses were conducted evaluating the interaction between DII score and selected factors (i.e. age below or more/equal than 65 years, the median value of the cohort; BMI below or more/equal than 30 kg m^{-2}; smoking status, categorised as previous/actual versus never) in the association with mortality, althoughb none emerged as moderator of our findings.

$P < 0.05$ was considered statistically significant. All analyses were performed using SPSS, version 21.0 (IBM Corp., Armonk, NY, USA).

Results

Study population

The MICOL III study initially included 1708 participants. After excluding 56 participants who did not have sufficient data for calculating the DII and 88 who did not have follow-up data, we retained a total of 1565 subjects for the final analysis (see Figure S1).

Mean (SD) age was 65.5 (9.5) years (range 43–89 years); 44.7% were women. The mean (SD) DII at baseline was –3.2 (1.5), with a range from –4.3 (higher-quality, anti-inflammatory diet) to +3.9 (lower-quality, pro-inflammatory diet). In the sample as a whole, the linear correlation between DII and aMED was weakly negative (Pearson's $P = -0.26$; $P < 0.0001$).

Baseline characteristics by tertiles of DII are provided in Table 1. Participants with higher DII scores (DII > 0.76, $n = 521$) were significantly older ($P = 0.007$) and were more likely to be male ($P < 0.0001$) than those with lower DII scores (DII < –0.83, $n = 522$) (Table 1). People with higher DII scores were more frequently smokers, and had a higher calorie and alcohol intake than people with lower DII scores. Finally, participants with higher DII scores reported a significantly lower incidence of diabetes ($P < 0.0001$) than those with lower DII scores. No differences were evident for other medical conditions investigated in the present study (Table 1).

Dietary inflammatory index and mortality

After a median follow-up period of 12 years, 366 participants (23.4% of the baseline population) died; 102 died from CVD and 87 from cancer. The overall mortality rate was 19 (95% CI = 17–21) per 1000 person-years.

Table 2 shows the associations between DII scores and mortality. Individuals with higher DII scores at baseline had a significant higher risk of mortality; data from survival curves confirm these findings (Fig. 1). After adjusting for 17 potential confounders (i.e. age, gender, demographics, comorbidities, dietary factors including aMED) at baseline and using the participants with lower DII scores as the reference group (DII < –0.83), individuals with a DII score between −0.83 and 0.76 had a 38% higher risk of overall mortality (HR = 1.38; 95% CI = 1.04–1.82; $P = 0.02$) and those in the highest category (DII ≥ 0.76) also had a 38% increase in risk (HR = 1.38; 95% CI = 1.03–1.86; $P = 0.03$) (Table 2). Based on the fully-adjusted model fit with DII as continuous, each increase in 1 SD (= 1.5 points) was associated with a significant 13% higher risk of overall mortality. None of the factors that have been hypothesised to affect DII scores (e.g. age, BMI, smoking status) emerged as a

Table 1 Descriptive characteristics of the study subjects by dietary inflammatory index, MICOL (Multicentrica Italiana COLeleitiasi) III Study, 2005–2017

	DII < –0.83 ($n = 522$)	DII –0.83 and 0.76 ($n = 522$)	DII > 0.76 ($n = 521$)	*P*-value*
Age (years)	64.4 (8.5)	66.2 (9.9)	65.9 (9.8)	0.007
Females (%)	53.6	45.2	35.1	<0.0001
General characteristics				
Smokers (previous/actual) (%)	41.8	42.1	49.5	0.01
BMI (kg m^{-2})	29.6 (5.4)	29.5 (5.2)	30.2 (5.4)	0.12
Systolic blood pressure (mmHg)	125 (20)	124 (21)	123 (20)	0.53
Diastolic blood pressure (mmHg)	75 (11)	74 (10)	75 (10)	0.42
Depressive symptoms score	28 (9)	27 (9)	27 (7)	0.41
Daily energy intake (kcal)	2099 (791)	2229 (758)	2232 (909)	0.01
Daily alcohol intake (g)	14.7 (20.5)	16.1 (20.9)	23.9 (26.1)	<0.0001
Comorbidities				
Diabetes (%)	18.8	13.6	10.4	<0.0001
Gastric ulcer (%)	13.4	14.6	11.9	0.47
Gallbladder stones (%)	13.4	16.7	13.1	0.88
Hepatic cirrhosis (%)	1.0	1.5	1.7	0.29
Previous cancer (%)	5.6	6.7	5.2	0.80
Acute myocardial infarction (%)	4.8	4.6	5.2	0.76
Score fatty liver	1.3 (1.8)	1.1 (1.7)	1.3 (1.8)	0.15

Values are reported as the mean (SD) (for continuous variables), or as a percentage for categorical ones.
**P* values were calculated using the analysis of variance for continuous variables and a chi-squared test for categorical variables, respectively.

Table 2 Association between dietary inflammatory index and mortality, MICOL (Multicentrica Italiana COLeleitiasi) III Study, 2005–2017

	Incidence of death (95% CI) per 1000 person-years	Basic adjusted HR† (95% CI)	*P*-value	Fully adjusted HR‡ (95% CI)	*P*-value
Overall mortality					
DII < –0.83	15 (12–18)	1 [reference]		1 [reference]	
DII –0.83 and 0.76	25 (21–30)	1.71 (1.31–2.23)	<0.0001	1.38 (1.04–1.82)	0.02
DII ≥ 0.76	24 (20–28)	1.61 (1.23–2.11)	0.001	1.38 (1.03–1.86)	0.03
Increase in 1 SD	–	1.18 (1.07–1.30)	0.001	1.13 (1.02–1.27)	0.03
Cardiovascular mortality					
DII < –0.83	4 (2–6)	1 [reference]		1 [reference]	
DII –0.83 and 0.76	7 (5–10)	2.02 (1.19–3.42)	0.009	1.52 (0.88–2.64)	0.13
DII ≥ 0.76	7 (5–10)	2.05 (1.21–3.47)	0.008	1.37 (0.77–2.46)	0.29
Increase in 1 SD	–	1.32 (1.10–1.59)	0.003	1.18 (0.95–1.45)	0.13
Cancer mortality					
DII < –0.83	4 (3–6)	1 [reference]		1 [reference]	
DII –0.83 and 0.76	5 (4–8)	1.31 (0.78–2.22)	0.31	1.06 (0.62–1.83)	0.83
DII ≥ 0.76	5 (4–8)	1.33 (0.79–2.26)	0.29	1.09 (0.61–1.93)	0.78
Increase in 1 SD	–	1.06 (0.87–1.29)	0.56	0.96 (0.77–1.21)	0.73

†Not adjusted.

‡Adjusted for age, sex, smoking status, diabetes, gastric ulcer, gallbladder stones, hepatic cirrhosis, cancer, acute myocardial infarction, body mass index, systolic and diastolic blood pressure, presence of depressive symptoms, presence of hepatic steatosis, energy and alcohol intake, and adherence to Mediterranean diet.

potential moderator of the association between DII and mortality (*P* for interaction for median age, 65 years = 0.87; for median BMI, 30 kg m^{-2} = 0.21; for smoking status = 0.16).

Table 2 also shows the association between DII scores at baseline and cause-specific mortality. Although the point estimates for CVD mortality were higher than for overall mortality in the fully adjusted model (e.g. 1.52 versus 1.38 in the third quartile), the confidence limits were wider and included 1.0. There was only a slight suggestion of increased risk for overall cancer mortality in the basic adjusted model and virtually no suggestion of increased risk in the fully adjusted model.

Discussion

In this ongoing prospective cohort of men and women living in a Mediterranean country, a higher DII score was

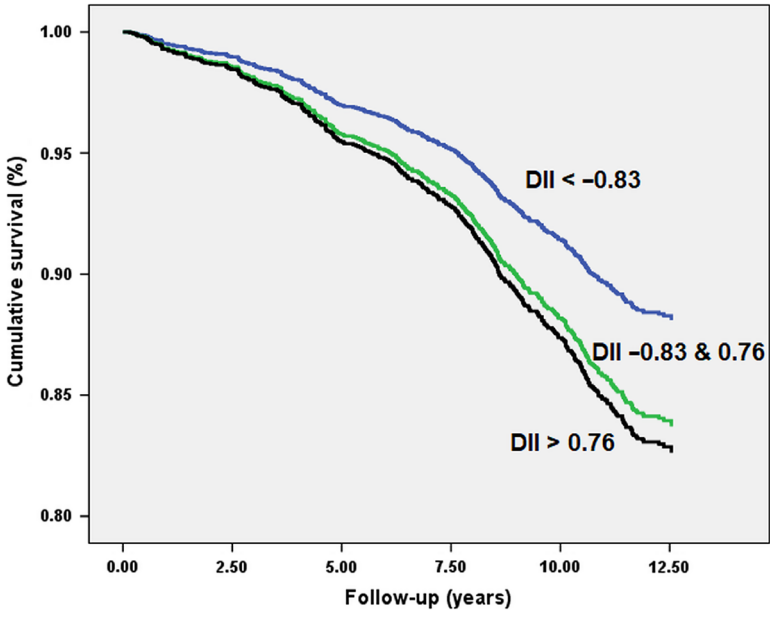

Figure 1 Survival curves by dietary inflammatory index scores at the baseline.

associated with an increased risk of all-cause mortality, independent of potential confounders. People with higher DII scores had an increased risk of mortality, even after adjusting for multiple confounding factors, including adherence to a Mediterranean diet. None of the factors that have been hypothesised to affect the DII, such as age, adiposity and smoking, influenced the association between DII and mortality. It is important to note the strong suggestion that risk was increased even more for cardiovascular disease mortality; however, confidence limits were wide because of imprecision as a result of a small sample size.

In a recent meta-analysis, the association between higher DII scores and all-cause mortality was significant, although this was characterised by a high heterogeneity and no specific strata that was included could explain the heterogeneity [14]. It could be that the DII is associated with a higher mortality risk probably because higher DII scores are associated with a higher incidence of some medical conditions *per se* rather than with mortality-specific factors [10,16,18,33–36]. For example, specific to the Italian region, DII has previously been shown to be associated with a variety of cancers [37,38] and acute myocardial infarction [39]. In relation to cancer-specific mortality, DII has been shown to be associated with prostate cancer [40] and digestive cancer mortality [41] but not with breast cancer mortality [42]. In a large randomised controlled trial, however, a pro-inflammatory diet was associated with an increased risk of all-cause mortality in the placebo group but not in the antioxidant-supplemented group, suggesting that inflammation and oxidative stress play an important role in determining mortality in human beings and that nutrients with antioxidant properties can counteract this effect [43].

The potential association between DII and increased risk of mortality can be explained via several mechanisms. First, the DII is significantly associated with low-grade inflammation [23] and higher CRP levels are associated with a higher risk for several cardiovascular conditions, including coronary heart disease and stroke, which increase the risk of mortality [44]. Second, higher DII scores reflect the higher consumption of foods traditionally associated with higher CVD risk, such as red meats [45], fats [46] and fried foods [(47)]. Similarly, higher DII scores reflect the lower consumption of vegetables and fruits that, by contrast, are associated with a lower CVD risk [48].

Our findings might have relevant clinical consequences. First, inflammation is a significant risk factor for important medical conditions ('inflammaging') [1] that are not only associated with a higher mortality risk, but also a with poorer quality of life.[49] Because the DII is linearly correlated with serum markers of inflammation [3–8], the possibility of modulating inflammation with a healthier diet that might provide important benefits for preventing mortality (particularly for CVD reasons) could be an important target of future intervention studies. Finally, we consider that our findings could be of importance in a Mediterranean country (such as Italy) in which adherence to healthy diet, such as the Mediterranean diet, is degrading year after year, as noted recently by a World Health Organization report [21]. In the only other report exploring DII and mortality in a Mediterranean population, after adjusting for a wide array of potential confounders, the comparison between extreme quartiles of the DII showed a positive and significant association with all-cause mortality in both the SUN cohort (HR = 1.42; 95% CI = 1.00–2.02; P_{trend} = 0.009) in Spain [22]. Although there are similarities in the dietary practices of people in Spain and Italy, there are some differences that warrant further study. For example, some classical Mediterranean foods, such as cereals and vegetables, were generally consumed more frequently by Italian students; others, such as fish and pulses, were generally consumed more frequently by Spanish students [50].

The findings of the present study should be interpreted within their limitations. First, the non-availability of data on several food parameters useful for calculating the DII should be considered. Some components (e.g. turmeric, saffron and eugenol) are not consumed in high quantity in this population, and so the non-availability of these food parameters may not have played major role in this association. However, the inclusion of parameters such as flavonoids, which are commonly consumed, may influence the results. Second, information regarding co-morbidities was self-reported and this could introduce an important bias. Finally, data regarding dietary habits were recorded only at the baseline; therefore, dietary changes made during the follow-up are not reflected in the results, particularly over 12 years of follow-up. However, this issue is common to other studies investigating DII and mortality [14].

In conclusion, the results of the present study suggest that higher DII scores are associated with a significantly higher mortality risk, also taking in account several confounders at the baseline, even if the data regarding specific-cause mortality are less clear. Our data may be particularly important because Mediterranean populations are transitioning toward less-healthy diets. This trend should be confirmed in future studies.

Conflict of interests, source of funding and authorship

The authors have no financial conflicts of interest to disclose. Dr James R. Hébert owns a controlling interest in Connecting Health

Innovations LLC (CHI), a company planning to license the right to his invention of the Dietary Inflammatory Index (DII) from the University of South Carolina aiming to develop computer and smartphone applications for patient counseling and dietary intervention in clinical settings. Dr Nitin Shivappa is an employee of CHI.
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NV, AMC, MN, RR, RI, OR and VT were responsible for drafting the paper. VG, AL, MC and GDL were responsible for statistical analysis. NS, JRH, GM, LF and MGC were responsible for critical revision.

Transparency declaration

The lead author affirms that this manuscript is an honest, accurate and transparent account of the study being reported. The reporting of this work is compliant with STROBE guidelines. The lead author affirms that no important aspects of the study have been omitted.

References

1. Franceschi C & Campisi J (2014) Chronic inflammation (inflammaging) and its potential contribution to age-associated diseases. *J Gerontol A Biol Sci Med Sci* **69**(Suppl 1), S4–S9.
2. Shivappa N, Steck SE, Hurley TG *et al.* (2014) Designing and developing a literature-derived, population-based dietary inflammatory index. *Public Health Nutr* **17**, 1689–1696.
3. Shivappa N, Steck SE, Hurley TG *et al.* (2014) A population-based dietary inflammatory index predicts levels of C-reactive protein in the Seasonal Variation of Blood Cholesterol Study (SEASONS). *Public Health Nutr* **17**, 1825–1833.
4. Tabung FK, Steck SE, Zhang J *et al.* (2015) Construct validation of the dietary inflammatory index among postmenopausal women. *Ann Epidemiol* **25**, 398–405.
5. Wirth MD, Shivappa N, Davis L *et al.* (2016) Construct validation of the Dietary Inflammatory Index among African Americans. *J Nutr Health Aging* 1–5.
6. Wirth MD, Burch J, Shivappa N *et al.* (2014) Association of a dietary inflammatory index with inflammatory indices and metabolic syndrome among police officers. *J Occup Environ Med* **56**, 986–989.
7. Ramallal R, Toledo E, Martinez-Gonzalez MA *et al.* (2015) Dietary inflammatory index and incidence of cardiovascular disease in the SUN cohort. *PLoS ONE*, **10, e0135221**.
8. Shivappa N, Hebert JR, Rietzschel ER *et al.* (2015) Associations between dietary inflammatory index and inflammatory markers in the Asklepios Study. *British J Nutr* **113**, 665–671.
9. Shivappa N, Bonaccio M, Hebert JR *et al.* (2018) Association of pro-inflammatory diet with low-grade inflammation: results from the moli-sani study. *Nutrition*.
10. Wood LG, Shivappa N, Berthon BS *et al.* (2015) Dietary inflammatory index is related to asthma risk, lung function and systemic inflammation in asthma. *Clin Exp Allergy* **45**, 177–183.
11. Shivappa N, Hebert JR, Marcos A *et al.* (2017) Association between dietary inflammatory index and inflammatory markers in the HELENA study. *Mol Nutr Food Res* **61**. https://doi.org/10.1002/mnfr.201600707
12. Neufcourt L, Assmann KE, Fezeu LK *et al.* (2015) Prospective association between the dietary inflammatory index and metabolic syndrome: findings from the SU.VI.MAX study. *Nutr Metab Cardiovasc Dis* **25**, 988–996.
13. Phillips CM, Shivappa N, Hebert JR *et al.* (2018) Dietary inflammatory index and biomarkers of lipoprotein metabolism, inflammation and glucose homeostasis in adults. *Nutrients* **10**, E1033.
14. Namazi N, Larijani B & Azadbakht L (2018) Dietary inflammatory index and its association with the risk of cardiovascular diseases, metabolic syndrome, and mortality: a systematic review and meta-analysis. *Horm Metab Res* **50**, 345–358.
15. Shivappa N, Godos J, Hebert JR *et al.* (2018) Dietary inflammatory index and cardiovascular risk and mortality-a meta-analysis. *Nutrients* **10**, E200.
16. Shivappa N, Godos J, Hebert JR *et al.* (2017) Dietary inflammatory index and colorectal cancer risk-a meta-analysis. *Nutrients* **9**, E1043.
17. Denova-Gutierrez E, Munoz-Aguirre P, Shivappa N *et al.* (2018) Dietary inflammatory index and type 2 diabetes mellitus in adults: the diabetes mellitus survey of mexico city. *Nutrients* **10**, E385.
18. Veronese N, Stubbs B, Koyanagi A *et al.* (2017) Pro-inflammatory dietary pattern is associated with fractures in women: an eight-year longitudinal cohort study. *Osteoporos Int* **29**, 143–151.
19. Deng FE, Shivappa N, Tang Y *et al.* (2017) Association between diet-related inflammation, all-cause, all-cancer, and cardiovascular disease mortality, with special focus on prediabetics: findings from NHANES III. *Eur J Nutr* **56**, 1085–1093.
20. Shivappa N, Hebert JR, Kivimaki M *et al.* (2017) Alternate Healthy Eating Index 2010, Dietary Inflammatory Index and risk of mortality: results from the Whitehall II cohort study and meta-analysis of previous Dietary Inflammatory Index and mortality studies. *British J Nutr* **118**, 210–221.
21. Europe WROf. What National and Subnational Interventions and Policies Based on Mediterranean and Nordic Diets Are Recommended Or Implemented in the Who European: Region and Is There Evidence of

Effectiveness in Reducing Noncommunicable Diseases? Geneva: World Health Organization; 2018.
22. Garcia-Arellano A, Martínez-González MA, Ramallal R *et al.* (2019) Dietary inflammatory index and all-cause mortality in large cohorts: the SUN and PREDIMED studies. *Clin Nutr* **38**, 1221–1231.
23. Shivappa N, Bonaccio M, Hebert JR *et al.* (2018) Association of proinflammatory diet with low-grade inflammation: results from the Moli-sani study. *Nutrition* **54**, 182–188.
24. Block G, Hartman AM & Naughton D (1990) A reduced dietary questionnaire: development and validation. *Epidemiology (Cambridge, Mass)* **1**, 58–64.
25. Gnagnarella, P.S., Salvini, S. & Parpinel, M. Food Composition Database for Epidemiological Studies in Italy 2015 [20 June 2018]. Available from: http://www.bda-ieo.it.
26. Willett WC, Howe GR & Kushi LH (1997) Adjustment for total energy intake in epidemiologic studies. *Am J Clin Nutr* **65**(4 Suppl), 1220S–1228S.
27. Trichopoulou A, Costacou T, Bamia C *et al.* (2003) Adherence to a Mediterranean diet and survival in a Greek population. *N Engl J Med* **348**, 2599–2608.
28. Zung WW (1965) A self-rating depression scale. *Arch Gen Psychiatry* **12**, 63–70.
29. Chiloiro M, Caruso MG, Cisternino AM *et al.* (2013) Ultrasound evaluation and correlates of fatty liver disease: a population study in a Mediterranean area. *Metab Syndr Relat Disord* **11**, 349–358.
30. Veronese N, Notarnicola M, Osella A *et al.* (2018) Menopause does not affect fatty liver severity in women: a population study in a Mediterranean area. *Endocr Metab Immune Disord Drug Targets* **18**, 513–521.
31. Jonckheere AR (1954) A distribution-free k-sample test against ordered alternatives. *Biometrika* **41**, 133–145.
32. Miles, J. *Tolerance and variance inflation factor*. Wiley StatsRef: Statistics Reference Online. 2009. https://doi.org/10.1002/9781118445112.stat06593
33. Shivappa N, Schoenaker DA, Hebert JR *et al.* (2016) Association between inflammatory potential of diet and risk of depression in middle-aged women: the Australian Longitudinal Study on Women's Health. *British J Nutr* **116**, 1077–1086.
34. Shivappa N, Stubbs B, Hebert JR *et al.* (2018) The relationship between the dietary inflammatory index and incident frailty: a longitudinal cohort study. *J Am Med Dir Assoc* **19**, 77–82.
35. Veronese N, Shivappa N, Stubbs B *et al.* (2019) The relationship between the dietary inflammatory index and prevalence of radiographic symptomatic osteoarthritis: data from the Osteoarthritis Initiative. *Eur J Nutr* **58**, 253–260.
36. Zhang ZQ, Cao WT, Shivappa N *et al.* (2017) Association between diet inflammatory index and osteoporotic hip fracture in elderly chinese population. *J Am Med Dir Assoc* **18**, 671–677.
37. Shivappa N, Hebert JR, Taborelli M *et al.* (2018) Association between dietary inflammatory index and Hodgkin's lymphoma in an Italian case-control study. *Nutrition* **53**, 43–48.
38. Shivappa N, Zucchetto A, Serraino D *et al.* (2015) Dietary inflammatory index and risk of esophageal squamous cell cancer in a case-control study from Italy. *Cancer Causes Control* **26**, 1439–1447.
39. Shivappa N, Tavani A, Hebert JR *et al.* (2018) Dietary inflammatory index and acute myocardial infarction in a large Italian case-control study. *Eur J Public Health* **28**, 161–166.
40. Zucchetto A, Gini A, Shivappa N *et al.* (2016) Dietary inflammatory index and prostate cancer survival. *Int J Cancer* **139**, 2398–2404.
41. Shivappa N, Steck SE, Hussey JR *et al.* (2017) Inflammatory potential of diet and all-cause, cardiovascular, and cancer mortality in National Health and Nutrition Examination Survey III Study. *Eur J Nutr* **56**, 683–692.
42. Zucchetto A, Serraino D, Shivappa N *et al.* (2017) Dietary inflammatory index before diagnosis and survival in an Italian cohort of women with breast cancer. *British J Nutr* **117**, 1456–1462.
43. Graffouillère L, Deschasaux M, Mariotti F *et al.* (2016) Prospective association between the Dietary Inflammatory Index and mortality: modulation by antioxidant supplementation in the SU.VI.MAX randomized controlled trial. *Am J Clin Nutr* **103**, 878–885.
44. Kaptoge S, Di Angelantonio E, Lowe G *et al.* (2010) C-reactive protein concentration and risk of coronary heart disease, stroke, and mortality: an individual participant meta-analysis. *Lancet (London, England)* **375**, 132–140.
45. Rohrmann S, Overvad K, Bueno-de-Mesquita HB *et al.* (2013) Meat consumption and mortality - results from the European Prospective Investigation into Cancer and Nutrition. *BMC Med* **11**, 63.
46. Keys A, Menotti A, Karvonen MJ *et al.* (1986) The diet and 15-year death rate in the seven countries study. *Am J Epidemiol* **124**, 903–915.
47. Veronese N, Stubbs B, Noale M *et al.* (2017) Fried potato consumption is associated with elevated mortality: an 8-year longitudinal cohort study. *Am J Clin Nutr* **106**, 162–167.
48. Veronese N, Solmi M, Caruso MG *et al.* (2018) Dietary fiber and health outcomes: an umbrella review of systematic reviews and meta-analyses. *Am J Clin Nutr* **107**, 436–444.
49. Murray CJL, Vos T, Lozano R *et al.* (2012) Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* **380**, 2197–2223.

50. Baldini M, Pasqui F, Bordoni A *et al.* (2009) Is the Mediterranean lifestyle still a reality? Evaluation of food consumption and energy expenditure in Italian and Spanish university students. *Public Health Nutr* **12**, 148–155.

Appendix

The MICOL study group includes: De Michele Giampiero, Mastrosimini Anna, Iacovazzi Palma, Laboratory of Clinic Pathology; Noviello Marisa, Unit of Radiology; Burattini Osvaldo, Unit of Gastroenterology II; D'Attoma Benedetta, Laboratory of Nutrional Phyisipathology, IRCCS Saverio de Bellis, Castellana G, Bari, Italy; and Pugliese Vittorio, Hospital of Monte Sant'Angelo, Putignano (BA).

Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Figure S1. Flow chart.