

# Influence of social determinants of health and county vaccination rates on machine learning models to predict COVID-19 case growth in Tennessee

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## ABSTRACT

**Introduction** The SARS-CoV-2 (COVID-19) pandemic has exposed health disparities throughout the USA, particularly among racial and ethnic minorities. As a result, there is a need for data-driven approaches to pinpoint the unique constellation of clinical and social determinants of health (SDOH) risk factors that give rise to poor patient outcomes following infection in US communities.

**Methods** We combined county-level COVID-19 testing data, COVID-19 vaccination rates and SDOH information in Tennessee. Between February and May 2021, we trained machine learning models on a semimonthly basis using these datasets to predict COVID-19 incidence in Tennessee counties. We then analyzed SDOH data features at each time point to rank the impact of each feature on model performance.

**Results** Our results indicate that COVID-19 vaccination rates play a crucial role in determining future COVID-19 disease risk. Beginning in mid-March 2021, higher vaccination rates significantly correlated with lower COVID-19 case growth predictions. Further, as the relative importance of COVID-19 vaccination data features grew, demographic SDOH features such as age, race and ethnicity decreased while the impact of socioeconomic and environmental factors, including access to healthcare and transportation, increased.

**Conclusion** Incorporating a data framework to track the evolving patterns of community-level SDOH risk factors could provide policy-makers with additional data resources to improve health equity and resilience to future public health emergencies.

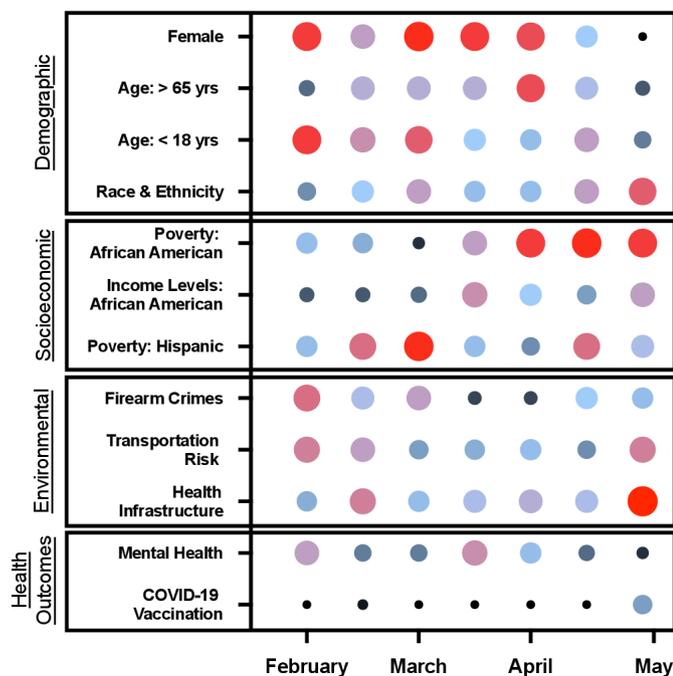
## INTRODUCTION

The SARS-CoV-2 (COVID-19) pandemic exacerbated health inequities throughout the USA, disproportionately affecting at-risk populations.<sup>1</sup> Identifying social determinants of health (SDOH) risk factors within US communities that contribute to poor outcomes following infection can improve health equity and strengthen community readiness for future public health emergencies.<sup>2 3</sup> Following vaccine roll-outs in 2021, we predicted Tennessee COVID-19

case growth using machine learning models and investigated the influence of SDOH factors on COVID-19 incidence to quantify and track opportunities to improve health equity.

## METHODS

Our approach combined publicly available COVID-19 testing, vaccination, hospitalization and death metrics with county-specific SDOH and demographic data.<sup>4 5</sup> Data sources included the Tennessee Department of Health, Johns Hopkins Coronavirus Research Center and the US Census database. We employed feature engineering and feature selection to identify novel predictors such as offset case counts to best represent changes in Tennessee county COVID-19 incidence between February and May 2021. We aggregated data from multiple sources to minimize implicit bias and removed or ignored missing values depending on the model type. An ensemble of generalized linear and tree-based machine learning models was built in parallel, each trained and tested with 4–6 weeks of historical COVID-19 case data to generate predictions from 40 to 50 models at 13 time points. Optimal models were selected using cross-validation metrics (eg, mean absolute error,  $R^2$ ) and prediction accuracy for future relative case growth normalized to county population.<sup>6</sup> We analyzed the impact of all features from top performing models to quantify and rank SDOH by their influence on COVID-19 incidence predictions. Finally, we calculated Pearson coefficients to quantify associations between vaccination rates and county COVID-19 case growth over time.



**Figure 1** Social determinants of health (SDOH) linked to COVID-19 case growth in Tennessee dynamically shift in importance over time. SDOH include social, physical and environmental factors that impact community health such as age, race, gender, access to transportation, access to primary care and community vaccination rates. Twelve of these SDOH features demonstrated the highest feature importance across all predictive models during the study period. Size and color are used to emphasize SDOH feature importance at each time point. Large, red (●) bubbles connote the top ranked SDOH feature while small dark blue (●) bubbles signify least importance of a given feature at each time point. Black bubbles (●) represent the least important feature at each time point compared with the other top ranked SDOH data elements.

## RESULTS

Machine learning models across all time points were more than 90% accurate when comparing model predictions to actual cases (online supplemental figure 1A and C). The top models demonstrated an average  $R^2$  value of 0.99, mean absolute error of 0.21 and 0.001 mean Tweedie deviance (online supplemental figure 1B).

Highly predictive SDOH features changed in importance over time. Categorically, demographic SDOH were most important in February 2021, but socioeconomic and environmental SDOH became increasingly more influential towards May. Health outcome SDOH features remained largely consistent during the study period. Individually, the female and under 18 age demographic features ranked highest in February and then declined while African American poverty and health infrastructure features, such as the number of hospital beds and community provider access statistics, increased in importance by mid-April. Lastly, COVID-19 vaccination data features grew in relative importance by May compared with the other SDOH factors (figure 1).

As Tennessee vaccination rates increased, counties with the lowest vaccination rates exhibited the highest COVID-19 case growth (online supplemental figure 2A). Initially, vaccination rates were not correlated with COVID-19 risk, but by mid-March, a statistically significant correlation with low risk of COVID-19 case growth emerged (online supplemental figure 2B).

## DISCUSSION

Efforts to curtail the health and economic impact of the SARS-CoV-2 pandemic illuminate the need to define specific risk factors that catalyze future case growth, worsen health disparities and adversely impact the public health response across US communities.<sup>7</sup> Addressing these challenges, we constructed a real-time predictive framework to discover and rank county-level SDOH risk factors that drive machine learning predictions of future COVID-19 incidence (figure 1).

In Tennessee, we found that communities with rapid vaccine roll-out were at lower risk for case growth (online supplemental figure 2). As vaccination levels began to rise, demographic SDOH features such as age, race and ethnicity declined in relative importance while socioeconomic and environmental risk factors such as poverty, access to transportation and healthcare infrastructure increased significantly. Measures promoting health equity rely on constant assessment of risk mitigation effectiveness. Real-time knowledge of community specific SDOH risk factors empowers healthcare organizations and local governments to improve policy and resource allocation to mitigate outbreaks, enhance resilience to future public health threats, and capture evolving risk profiles as novel virus variants emerge.<sup>8</sup>

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**Competing interests** LSW, JDG and CFS are shareholders in IQuity Labs (Nashville, Tennessee, USA) and Decode Health (Nashville, Tennessee, USA). IQuity Labs develops blood-based RNA tools to aid in the diagnosis and treatment of human disease. Decode Health develops artificial intelligence approaches to predict chronic and infectious disease risk in patient populations.

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# Implementation of a non-emergent medical transportation programme at an integrated health system

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## ABSTRACT

**Objectives** To implement a unified non-emergency medical transportation (NEMT) service across a large integrated healthcare delivery network.

**Methods** We assessed needs among key organisational stakeholders, then reviewed proposals. We selected a single NEMT vendor best aligned with organisational priorities and implemented this solution system-wide.

**Results** Our vendor's hybrid approach combined rideshares with contracted vehicles able to serve patients with equipment and other needs. After 6195 rides in the first year, we observed shorter wait times and lower costs compared with our prior state.

**Discussion** Essential lessons included (1) understanding user and patient needs, (2) obtaining complete, accurate and comprehensive baseline data and (3) adapting existing workflows—rather than designing de novo—whenever possible.

**Conclusions** Our implementation of a single-vendor NEMT solution validates the need for NEMT at large healthcare organisations, geographical challenges to establishing NEMT organisation-wide, and the importance of baseline data and stakeholder engagement.

## INTRODUCTION

Non-emergency medical transportation (NEMT)—to medical appointments, to urgent care services or home from the hospital—represents a barrier to healthcare for almost 6 million individuals in the USA.<sup>1</sup> Obstacles include cost, accessibility (eg, wheelchair-accessible vehicles), local availability and reliability, which are associated with care delays, worse health outcomes and increased costs.<sup>2</sup>

NEMT is an important social determinant of health.<sup>3,4</sup> Unsurprisingly, transportation barriers are commonly experienced by low-income patients and racial and ethnic minority patients, propagating healthcare inequities.<sup>2</sup> Additionally, NEMT causes suboptimal patient and staff experiences through complex advanced scheduling procedures, long waits and missed appointments.<sup>5</sup> Further, although Medicaid beneficiaries are entitled to NEMT in certain circumstances, options

for other patients are limited and heterogeneous at the system level.

Recently, alternative strategies, such as rideshare-based NEMT systems, have improved outcomes including appointment show-rates, general wait times and cost.<sup>6,7</sup> Here, we describe our development and implementation of a unified NEMT service across a large integrated healthcare delivery network.

## METHODS

We conducted this work at BJC HealthCare, an integrated network of 15 hospitals including a 1300-bed urban quaternary hospital (Barnes Jewish Hospital, the teaching hospital of Washington University School of Medicine), several 500-bed community hospitals and multiple smaller community hospitals in Missouri and Illinois.

First, we conducted a needs assessment in early 2019 to (1) establish a shared understanding of our organisation's NEMT needs, (2) prioritise vendor capabilities and (3) establish baseline measurements and define key results necessary for success. To align our understanding of the problem with that of our key stakeholders, we engaged front-line care managers and social workers to empathise with the patient and staff NEMT experience. We also involved organisational legal and compliance experts to frame potential solutions, around anti-inducement regulations.<sup>8</sup> We proactively adopted the institutional stance that all NEMT would occur within the boundaries of safe harbours.

Second, we requested proposals through our centralised procurement division. [Table 1](#) lists our priorities. Our proposal-vetting team included the stakeholders named above.

Our implementation plan was sequential (ie, hospital by hospital) through an initial information security risk assessment,

**Table 1** Organisational priorities for an NEMT vendor

| Priority              | Comment   |
|-----------------------|---|
| Single vendor         | Vendor capable of supporting current and future ride volume across entire organisation                                |
| Ride capabilities     | Vendor capable of transporting both ambulatory and special patient/equipment needs (eg, wheelchairs)                  |
| Scheduling            | Vendor capable of supporting both prearranged and on-demand single-way (eg, discharges) and round-trip transportation |
| Experience            | Vendor willing to commit to maximising the quality of patient and staff experience                                    |
| Cost                  | Vendor offers competitive price point   |
| Data driven           | Vendor routinely provides data and insight at both system and unit level  |
| Regulatory compliance | HIPAA compliant   |

HIPAA, Health Insurance Portability and Accountability Act; NEMT, non-emergency medical transportation.

contracting and a stepwise launch. Key success measures included complete system-wide ride availability regardless of patient locale, continuous scheduling platform availability, time spent scheduling rides, wait times and cost.

## RESULTS

### Needs assessment

Through a mix of expenditure data, voucher counts and unit reports, our needs assessment estimated over 16 000 yearly rides within our organisation, mostly through taxicab vouchers, wheelchair-capable vans or idle ambulances. Most rides were hospital or emergency-department discharges (n=4764, 65%). We identified multiple problems related to NEMT (online supplemental table 2), which collectively indicated the need for system-wide NEMT redesign. For example, taxi rides were organised and funded by individual units, without any system to support or track data on this need; this lack of data precluded comparisons between the new platform and the prior system. Social workers—the main ride organisers—relied on foundation support or petty cash, which were inherently unstable. Financially, NEMT was deemed a system priority because of the potential for downstream cost savings (eg, through reducing no-show appointments). With the exception of Medicaid-funded hospital discharge rides, other NEMT resources were financed locally through grants.

### Proposal evaluation

Six vendors submitted proposals; after initial review, the four vendors able to meet our system's volume needs were given full consideration. Using a structured review template based on the priorities in table 1, our broad stakeholder group ultimately selected Kaizen Health (Chicago, Illinois, USA), a healthcare logistics entity focused on NEMT. Kaizen Health's hybrid approach merges software-based rideshare integration with call centre-managed traditional transportation options. As compared with other finalists, Kaizen Health demonstrated superior ability to provide a mix of rural and urban coverage and special needs rides, and to leverage utilisation data for organisational planning.

### Implementation

Although rideshare services were immediately available, these incompletely met our need for specialised medical transport. We experienced delays initiating services such as wheelchair and bariatric support; Kaizen first needed to establish agreements with local transportation providers for these specialised rides. This barrier was particularly challenging in rural areas, where there is little rideshare availability and few companies able to cover the requisite geographic footprint. Addressing these barriers added 6 weeks to the implementation timeline, but was a one-time effort.

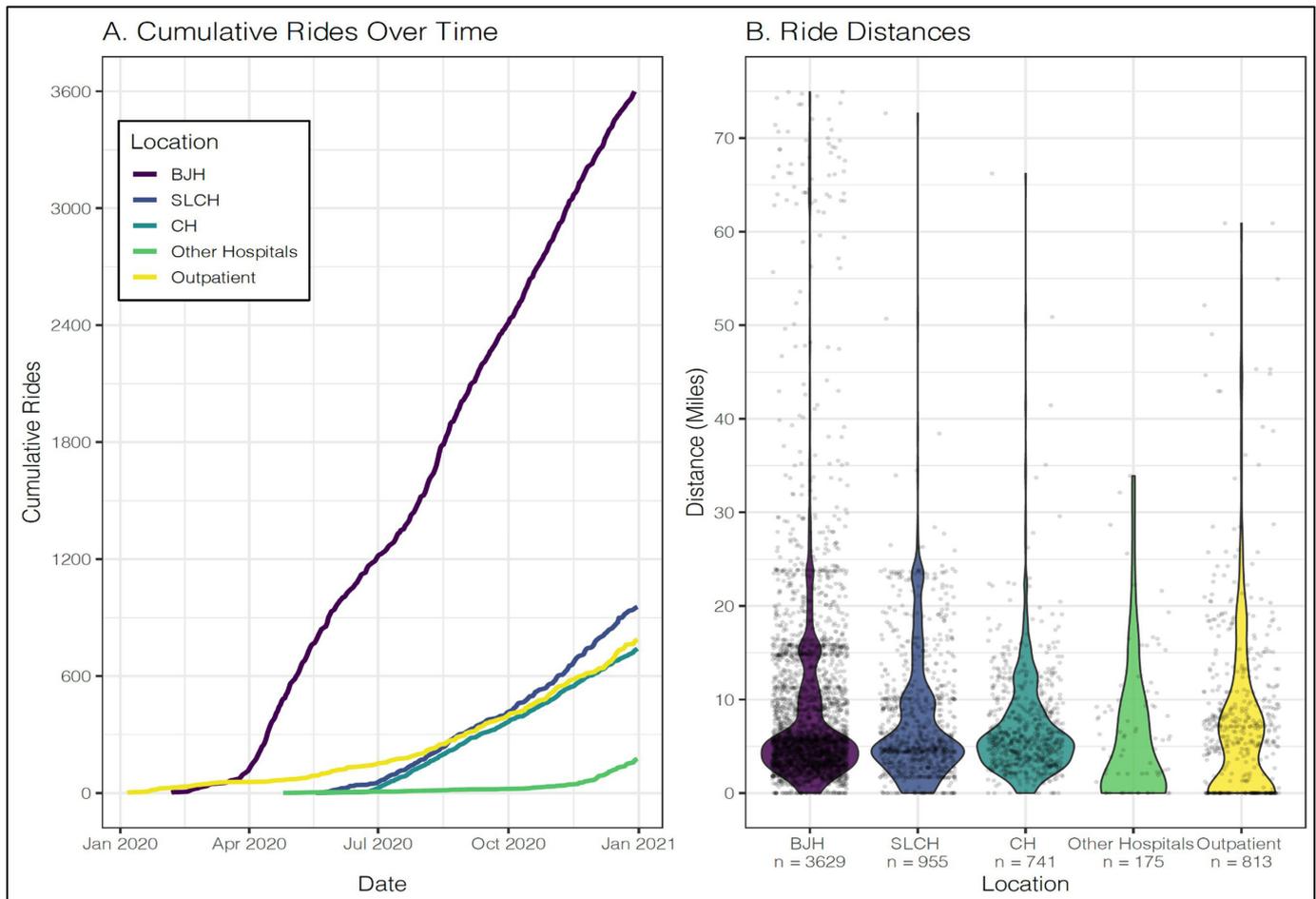
Staff engaged with Kaizen's platform through a web portal (online supplemental figure 1), through which they contacted a Kaizen broker to identify transportation options based on capacity, ability to serve the required service level and availability. The broker would finalise a ride via automatic software or manual confirmation (depending on the type of transportation), but the user experience remained the same regardless of transportation type.

### Evaluation

Kaizen Health provided 6195 rides from 3633 patients in 2020 (figure 1A). NEMT patients tended to be young, to self-identify as black, and to reside in zip codes with high Area Deprivation Indices (online supplemental table 3).

Most rides (5545, 88%) were rideshares and almost two-thirds (4188, 66%) were for hospital discharge (online supplemental table 4). In general, rides were short (median distance 5.4 miles (IQR 3.2–10.0 miles), although 142 rides (2.3%) exceeded 50 miles (figure 1B). For just-in-time calls, waits were typically under 10 min. By contrast, social workers reported waits of 30 min to several hours prior to our NEMT update. Compared with taxicab voucher outlay in 2019, the Kaizen Health NEMT programme incurred approximately US\$114 000 lower costs in 2020.

We surveyed workers arranging transportation. Of 153 workers approached, 44 (29%) responded. Respondents characterised the new platform as easier to use (n=34, 77%), as fast or faster for scheduling (n=39, 91%) and



**Figure 1** (A) Shows cumulative ride use over time across different sites within our system. (B) Shows site-specific individual ride distances (grey points) and their overall distribution (violin plots). BJH, Barnes Jewish Hospital; SLCH, St. Louis Children's Hospital; CH, Christian Hospital.

as fast or faster for ride arrival ( $n=40$ , 93%) than prior NEMT experiences. Informal shadowing and patient anecdotes provided by staff suggested that patient experience was improved by decreased wait times and fewer cancellations.

## DISCUSSION

We implemented a single-vendor NEMT solution across our system, identifying positive returns on the initial investment in terms of patient and staff experience, ride-related delays and costs.

Limitations include confounding in ride numbers and patient mix due to COVID-19. However, this challenge also demonstrated the robustness and flexibility of our vendor's platform, which allowed us to meet an immediate need by organising dedicated COVID-19 NEMT rides. Additionally, because a key aspect of our intervention involved systematic data collection, we were unable to generate an otherwise-equivalent control group for comparison. We partially mitigate this issue through historical comparisons.

Our work also has strengths. First, we evaluated, selected and implemented our solution rapidly, showing

the effectiveness of an organised approach to innovation. Second, we demonstrated the feasibility and benefits of implementing a single-vendor system across a large healthcare system. Despite early challenges in rural availability, we met a diverse range of patients' needs. Third, we captured previously unrecorded data—such as ride wait times—to allow quality control and future improvements.

We identified important lessons relevant for organisations considering NEMT programmes. First, identifying rural transportation was challenging. Our service could have launched earlier, and more smoothly, if we had better understood our patients' needs up front. To create a local transportation network, the vendor needed accurate estimates of expected volume, patient needs and county-level origins and destinations. Advance preparation of this information could have allowed the vendor to curate a focused list of potential partners.

Second, we validated the importance of accurate and comprehensive baseline data. Our ability to demonstrate success was limited by unavailable baseline direct (eg, number of no-show taxicabs) and indirect (eg, time from discharge to hospital departure) measures of success.



Third, our solution was most successful in the units with existing taxicab-hailing workflows. Adapting workflows appears less burdensome than designing workflows de novo, which requires deliberate consideration of oversight, budgeting, patient eligibility, staff capabilities and ‘ownership’ of day-to-day responsibilities. Tiered implementation with ‘soft’ launches allowed staff to become familiar with the new process, while allowing us to adapt best practices for implementation at the next site.

## CONCLUSIONS

Our implementation of a single-vendor NEMT solution validates the need for NEMT at large healthcare organisations, geographical risks to establishing a feasible and available NEMT solution organisation-wide, and the importance of baseline data and stakeholder engagement.

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**Contributors** PGL, BAR, MW, MG, JKE, AK and TMM have substantial contributions to the conception and design of the work; the acquisition, analysis and interpretation of data for the work, drafted the work and revised it critically for important intellectual content; provided final approval of the version to be published; and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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# Generating insights in uncharted territories: real-time learning from data in critically ill patients—an implementer report

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## ABSTRACT

**Introduction** In the current situation, clinical patient data are often siloed in multiple hospital information systems. Especially in the intensive care unit (ICU), large volumes of clinical data are routinely collected through continuous patient monitoring. Although these data often contain useful information for clinical decision making, they are not frequently used to improve quality of care. During, but also after, pressing times, data-driven methods can be used to mine treatment patterns from clinical data to determine the best treatment options from a hospital's own clinical data.

**Methods** In this implementer report, we describe how we implemented a data infrastructure that enabled us to learn in real time from consecutive COVID-19 ICU admissions. In addition, we explain our step-by-step multidisciplinary approach to establish such a data infrastructure.

**Conclusion** By sharing our steps and approach, we aim to inspire others, in and outside ICU walls, to make more efficient use of data at hand, now and in the future.

(eg, artificial intelligence) can be helpful by mining large volumes of data and discover clinical patterns and best treatment options from clinical data.<sup>3,4</sup>

Immediately after the outbreak, several initiatives such as the Dutch Data Warehouse and the covidpredict initiative were announced aiming to collect large amounts of data on COVID-19 ICU patients to eventually optimise clinical care and improve outcome.<sup>5</sup> However, the collection and organisation of data from multiple ICUs is time consuming and is often obstructed by technical and privacy challenges.<sup>6</sup> Furthermore, the agglomeration of data is unresponsive to local variations in population or disease-specific patterns, and different local practices and clinical definitions impede proper comparison between cohorts.<sup>7</sup>

Given these considerations, we aimed to implement a local data infrastructure that would enable us to learn in real time from our own consecutive COVID-19 ICU admissions by comparing patient characteristics, treatment regimens and clinical outcomes. Here, we present how a structured data approach can help to improve quality of care and can serve as a basis for advanced data analysis.

## Implementing a real-time clinical data infrastructure

All consecutive patients with COVID-19 admitted to the adult ICU of the Erasmus University Medical Center, a tertiary referral centre in Rotterdam, The Netherlands, were analysed. The need for written informed consent was waived by the regional medical research ethics committee. [Figure 1](#) provides a week-by-week overview of the data infrastructure development process along with the engaged stakeholders.

## INTRODUCTION

The current pandemic demonstrated that healthcare was in uncharted territory. As such, the outbreak of the novel COVID-19 could be a turning point for the initiation of advanced analytics, especially in intensive care medicine. The pandemic emphasized the importance of instant, or even real time, analysis of large volumes of intensive care unit (ICU) data in order to generate new insights to eventually improve quality of care.<sup>1</sup>

The ICU typically is an environment where clinicians are confronted with large amounts of clinical data siloed in multiple information systems and are often not optimally used to aid clinical decision making.<sup>2</sup> Even more, data are often collected when dealing with complex diseases or conditions to improve understanding of the clinical course and to evaluate the effects of therapeutic interventions at a later stage. However, especially in pressing times, advanced data analytics tools



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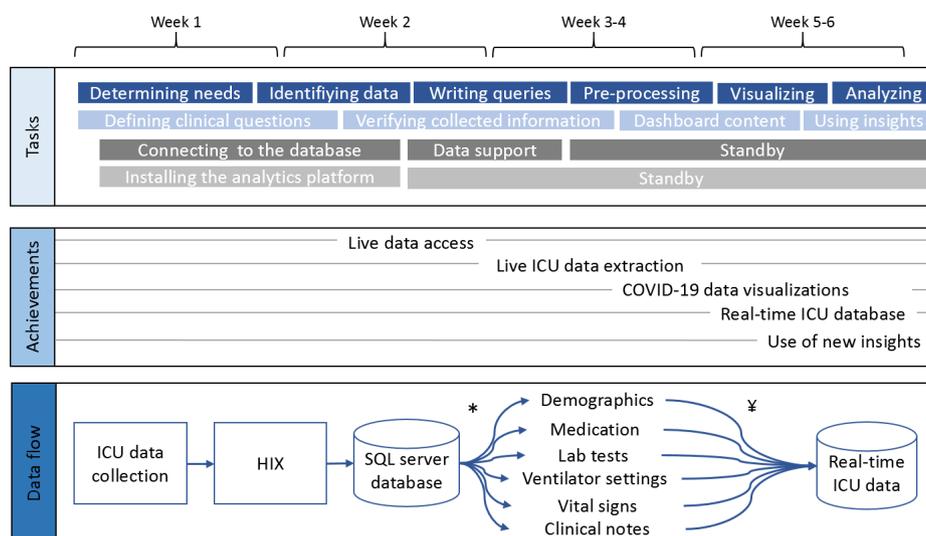
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**Figure 1** Road towards a real-time clinical data infrastructure. Stakeholders were engaged early in the process and tasks were distributed (dark blue=ICU research team, light blue=ICU physicians, dark grey=data and analytics department and light grey=IT department). After 6 weeks, a data infrastructure was implemented that allows to extract data in real-time from the electronic health record (HIX). \*Demographics, medication, lab tests, ventilator settings, vital signs and clinical notes were extracted from the database using structured query language (SQL) in Microsoft SQL management Studio. ¥The analytics platform, SAS Viya (V.8.3) was used to process and further analyse the data. Figure 1 was created by the lead author, and permission to reuse the image was obtained. HIX, Healthcare Information eXchange; ICU, intensive care unit; IT, information technology.

From start, a weekly recurring meeting was scheduled with the local information technology (IT) department, the data and analytics department and a third software party (SAS Institute, Cary, North Carolina, USA). Clinical questions and needs were formulated and determined in collaboration with a team of ICU physicians. Physicians were particularly interested in the treatment effect of several interventions, such as the effect of prone positioning, effect of high or low dose steroids, timing of steroids and the influence of body mass index on several outcome parameters, such as survival and mechanical ventilation days, in these critically ill patients. In our hospital, all patient data from the electronic health record (EHR), Healthcare Information eXchange (HIX), are routinely stored in a structured query language (SQL) server database (referred to as 'database'). Since these data originate from a single source, it was already properly formatted (data engineering) and did not need additional harmonisation. As such, the data and analytics department established a live connection to the database server (by using Microsoft SQL management studio) for qualified members of the ICU research team with restricted access to ICU patients. Subsequently, the IT department installed a data analytics platform (SAS Viya V.8.3) to ensure data extraction, data management, facilitate data visualisation and advanced analytics, and data and model governance.

In the second week, relevant data were identified in the database (figure 1), and SQL queries were written to extract these data, supervised by a senior data analyst. The data and analytics department provided support throughout the data identification and extraction process.

Extracted data were continuously verified with the team of ICU physicians to ensure its completeness.

From the third to the fourth week tables containing raw data were joined from separate queries and processed using SAS programming language. To be able to cope with the rapidly growing number of patients with COVID-19, ICU capacity expanded from 45 to 102 beds in a matter of days, mostly towards other parts of the hospital. To oversee patient characteristics in multiple ICU locations, a real-time 'COVID-19 clinical data dashboard' was required and was developed in the fifth week. Since then, the data were further processed, and in the sixth week, a research database was constructed that could be used to perform in-depth advanced analysis.

### Analysing clinical data in real time

A dashboard was successfully constructed containing information regarding patient demographics (such as gender, age and body mass index), treatment (such as prone positioning, optimal positive end-expiratory pressure titration and steroids (yes/no)), complications (such as pulmonary aspergillosis) and outcome (such as ventilator-free days and ICU mortality). Real-time availability of these data via the dashboard provided us with the opportunity to quickly reflect on treatment regimens and clinical outcomes, without the need to await findings from national and international database studies. To optimise its usefulness to continuously drive care improvement, we implemented a plan-do-check-act procedure. Clinical outcomes of the different treatment protocols were continuously analysed and discussed during a weekly meeting, and amended if necessary ('plan').

Protocol adjustments ('do') were closely monitored using the data infrastructure and the dashboard with a continuous real time data feed ('check'). Results were evaluated during the weekly meeting or earlier when needed, and outcomes and possible additional actions were discussed ('act'). This infrastructure enabled us to detect the high incidence of pulmonary embolisms in patients with COVID-19, the first group in the Netherlands, and more recently, it contributed to adaptations in our local COVID-19 ICU treatment protocols leading to implementation of a pulse dose intravenous methylprednisolone.<sup>8–10</sup> As such, we believe that structuring and organizing these vast amounts of clinical data on a local level is fundamental to leverage data analytics to improve quality of care.

Currently, 19 August 2021, the research database contains information of 546 COVID-19 ICU patients and increasing, with an overall mortality of 22.9% (125 patients), 69% were male (377 patients) and median age is 63 years (IQR 54–69). The data infrastructure is organised in such a way that it is automatically updated (by means of the scheduled SQL jobs in SAS Viya), facilitating continuous real-time data analysis in order to answer urgent clinical questions. To date, the data infrastructure is limited to EHR data and will therefore be enriched with data from multiple information systems (imaging, microbiology and bedside monitors) to warrant future use.

## CONCLUSION

We demonstrate the successful development of a real-time data infrastructure that enabled both data-driven care and decision making and rapid answering of critical clinical questions during pressing times, such as the COVID-19 pandemic. Although this data infrastructure was developed in the ICU, the underlying process could be extrapolated to other specialties to enable real-time data analysis to eventually improve quality of care.<sup>2</sup> By sharing our steps and clinical use, we aim to inspire others to make more efficient use of the data at hand, now and in the future.

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# Evaluating risk stratification scoring systems to predict mortality in patients with COVID-19

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## ABSTRACT

**Background** The COVID-19 pandemic has necessitated efficient and accurate triaging of patients for more effective allocation of resources and treatment.

**Objectives** The objectives are to investigate parameters and risk stratification tools that can be applied to predict mortality within 90 days of hospital admission in patients with COVID-19.

**Methods** A literature search of original studies assessing systems and parameters predicting mortality of patients with COVID-19 was conducted using MEDLINE and EMBASE.

**Results** 589 titles were screened, and 76 studies were found investigating the prognostic ability of 16 existing scoring systems (area under the receiving operator curve (AUROC) range: 0.550–0.966), 38 newly developed COVID-19-specific prognostic systems (AUROC range: 0.6400–0.9940), 15 artificial intelligence (AI) models (AUROC range: 0.840–0.955) and 16 studies on novel blood parameters and imaging.

**Discussion** Current scoring systems generally underestimate mortality, with the highest AUROC values found for APACHE II and the lowest for SMART-COP. Systems featuring heavier weighting on respiratory parameters were more predictive than those assessing other systems. Cardiac biomarkers and CT chest scans were the most commonly studied novel parameters and were independently associated with mortality, suggesting potential for implementation into model development. All types of AI modelling systems showed high abilities to predict mortality, although none had notably higher AUROC values than COVID-19-specific prediction models. All models were found to have bias, including lack of prospective studies, small sample sizes, single-centre data collection and lack of external validation.

**Conclusion** The single parameters established within this review would be useful to look at in future prognostic models in terms of the predictive capacity their combined effect may harness.

## INTRODUCTION

The SARS-CoV-2 outbreak has put enormous strain on healthcare systems around the world. According to the WHO, as of 12 January 2021, there have been more than 91 million cases of COVID-19 reported worldwide, with almost 2 million deaths.<sup>1</sup> To properly allocate resources and aid clinical decision-making,

there is an urgent need for a simple, accurate system to rapidly identify patients who are at the highest risk of death.

Traditionally, scoring systems are used in healthcare to stratify risk, predict outcomes and appropriately manage patients.<sup>2</sup> For example, the CRB-65 scoring system is efficiently used to assess the mortality risk of pneumonia in primary care to determine the need for management escalation.<sup>3</sup>

Risk stratification methods have been effectively used in previous viral outbreaks such as the Ebola epidemic in 2014 to reduce casualties.<sup>4</sup> With COVID-19 being a novel disease, no pre-existing risk stratification methods were available, so traditional scoring systems were adapted in the early stages of the pandemic. As the pandemic progressed, COVID-19-specific tools were developed by studying patients' characteristics relating strongly to mortality and incorporating them into scoring systems.

Although artificial intelligence (AI) algorithm development varies depending on the number of possible outcomes, it is an ideal way of stratifying patients.<sup>5</sup> It uses dynamic data and continual updating of its algorithm to increase the accuracy of its predictions.

This review aims to provide a summary of the literature available on risk stratification tools, including prediction models and single parameters used to predict the mortality of patients with COVID-19 to aid clinical decision-making. This review also aims to evaluate the applications of AI in mortality prediction models.

This study hopes to fill in the gaps in the current literature reviewing human and AI scoring tools. In addition, new studies investigating parameters associated with SARS-CoV-2 mortality are being published; therefore, constant evaluation of risk stratification tools is imperative in a rapidly evolving pandemic.



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**Table 1** Database search strategy of MEDLINE and EMBASE for the period January 2019 to 5 January 2021

| COVID-19 (TI, AB, KW)                           | Risk stratification (TI, AB, KW)                      | Mortality (TI, AB, KW)    |
|---|---|---------------------------|
| COVID-19  | Prognos*4 adj2 model/score/algorithm /tool            | Hospital Mortality (MeSH) |
| COVID-2019                                      | Clinical decision tool                                | Death*1                   |
| SARS-CoV-2                                      | Predicti* adj2 model/score/algorithm /tool            | Mortality                 |
| Severe acute respiratory syndrome coronavirus 2 | Risk adj2 model / predicti*/score/tool/stratification | Fatal*5                   |
| 2019-nCoV                                       | Scor*3 system*1<br>Mortality adj1 scor*3              |                           |

The following search concepts were combined using Boolean operators: COVID-19 (TI, AB, KW) AND Risk stratification (TI, AB, KW) AND Mortality (TI, AB, KW)  
AB, abstract; KW, keywords; TI, title, the '/' indicated a different variation.

## METHODS

A comprehensive search of MEDLINE and EMBASE between 1 January 2019 and 5 January 2021 was conducted to retrieve studies related to mortality risk prediction of patients with COVID-19. The search was done using the keywords and relevant MeSH terms displayed in [table 1](#).

Inclusion criteria were the following: (1) primary studies carried out on adult patients who are COVID-19-positive; (2) reporting of a model for predicting mortality with a reported area under the receiving operator curve (AUROC) value; and (3) routine blood or imaging parameters with mortality as the main outcome of interest. The established definition of AUROC applied to the context of a COVID-19 mortality prediction model was used; the accuracy of the model was used to discriminate the mortality risk levels in patients with COVID-19.<sup>6</sup>

Exclusion criteria were non-English studies, sample size <100 patients and non-peer-reviewed publications. Any disagreements during screening were resolved by consensus. Mortality, for this review, is defined as death within 90 days of hospital admission due to COVID-19.

A data extraction form was generated to synthesise the following information: study title, method of calculation of the model or examined parameters (eg, statistical modelling or analysis, AI), scoring system versus analysis of single parameters, 'summary of included parameters and AUROC for scoring systems', 'name and category of parameter (eg, biomarker)' for single parameters and any additional salient findings.

## RESULTS

After deduplication of original search results, title and abstracts of 589 studies were screened for relevance, and subsequently full-text articles were obtained and further

assessed for eligibility. In all, 76 studies were identified that would inform our review.

### Adapted current scoring systems

The sudden arrival of the pandemic has necessitated the application of existing prognostic systems to triage the influx of patients with COVID-19 to optimise distribution of limited resources and treatment. The accuracy of scoring systems adapted for COVID-19 mortality is detailed in online supplemental table 1 and then analysed to explore potential reasons for their differing predictive ability of mortality in patients with COVID-19.

Scoring systems are listed in order of descending AUROC values, as methodical differences between studies deem it inappropriate to merge AUROC results. For example, the *Quick Sequential Organ Function Assessment* (qSOFA) AUROC values ranged from 0.6200 to 0.8860 (online supplemental table 1), possibly due to different cut-off points. In addition, mortality was measured by 72 hours in some studies and up to 90 days in others, and sample sizes ranged from 105 to 864 across studies (online supplemental table 1).

The *Acute Physiology and Chronic Health Evaluation II* (APACHE II) score was found to have the highest AUROC values, followed by *Modified Elixhauser Index* (mEI) and *Sequential Organ Function Assessment* (SOFA) systems. APACHE II presides over other scores in terms of mortality prediction possibly due to its consideration of both age and comorbidities, whereas scores such as CURB-65 only assesses age and SOFA involves neither. Notably, however, the cut-off value for APACHE II is much lower when applied to patients with COVID-19 than under normal intensive care unit (ICU) conditions; while *Glasgow Coma Scale* (GCS) is an important component of APACHE II, the nervous system is typically less impacted than the respiratory system in COVID-19 infection.<sup>7</sup>

### COVID-19 scoring systems

Prediction scores play a vital role in guiding clinical decision-making for hospitalised patients with COVID-19. Online supplemental table 2 summarises recently developed scores and their AUROC values.

Different risk stratification tools use a variety of parameters to predict mortality. Online supplemental table 3 summarises the most common parameters used in novel COVID-19 mortality prediction scores. The two parameters associated with high predictive performance (higher AUROC) were lymphocyte count and D-dimer, with age being the most consistently used parameter. The most common parameter used in novel prediction models for mortality of patients with COVID-19 is age, followed by lymphocyte count, D-dimer, oxygen saturation, C reactive protein (CRP) and platelet count. Other less common parameters include respiratory rate (RR), lactate dehydrogenase, neutrophil-to-lymphocyte ratio (NLR), procalcitonin (PCT) and blood urea nitrogen.

The most common comorbidities for predicting mortality are hypertension (HTN), diabetes mellitus

(DM), obesity, cardiovascular disease, chronic kidney disease, smoking and malignancy.

### Single parameters

COVID-19 has a different clinical picture to pneumonia and influenza, providing an avenue to explore what routinely available clinical information best predicts mortality. We explored blood parameters and imaging not currently extensively implemented into existing COVID-19 mortality prediction models, which are represented in online supplemental table 4.

Studies examining the associations of a range of laboratory biochemical tests and imaging at admission with mortality for patients with COVID-19 are extensive in the literature. Continued rapid identification of biomarkers that can accurately predict the likelihood of mortality is essential and has been proposed, including inflammatory, coagulation, renal, liver and cardiac biomarkers (online supplemental table 4).

Imaging, particularly chest CT scans, has been studied, with all three studies reporting independent associations with mortality, shown in online supplemental table 5. Alongside prognostic scores developed to assess risk of death, these must be updated to reflect the identification of imaging modalities that may need to be added or replace parameters in existing scores.

### AI in predicting mortality

Machine learning (ML) is a subset of AI allowing systems to automatically improve based on new experiences.<sup>8</sup> Online supplemental table 6 illustrates an overview of studies that used ML to predict mortality in patients with COVID-19.

Papers that used ML models have an AUROC greater than 0.8, conveying good discrimination of patients with high mortality risk.<sup>6</sup>

Models with a greater number of incorporated parameters did not find improvements in AUROC score. One model by Yuan *et al*<sup>9</sup> had a high AUROC of 0.9551 when looking at three parameters, while the model by Vaid *et al*<sup>10</sup> had a lower AUROC of 0.8400 when looking at 73 different parameters. This suggests that the total number of parameters was a less important factor than the interaction between the parameters in predicting mortality.

Deep learning (DL) is a subset of ML which uses algorithms to analyse multiple factors simultaneously<sup>11</sup>; therefore, it would be more appropriate to handle multiple parameters. Online supplemental table 7 illustrates an overview of the studies that used ML to predict mortality in patients with COVID-19.

There are fewer studies assessing DL models, but similar to ML, these studies possess an AUROC >0.8.

## DISCUSSION

### Adapted current scoring systems

The variables used within existing scoring systems featured in online supplemental table 1 were analysed

to explore potential reasons for their differing predictive ability of mortality in patients with COVID-19.

The APACHE II score was found to have the highest AUROC values, followed by mEI and SOFA systems. APACHE II presides over other scores in terms of mortality prediction possibly due to its consideration of both age and comorbidities, whereas scores such as CURB-65 only assesses age and SOFA involves neither. Notably, however, the cut-off value for APACHE II is much lower when applied to patients with COVID-19 than under normal ICU conditions; while GCS is an important component of APACHE II, the nervous system is typically less impacted than the respiratory system in COVID-19 infection.<sup>7</sup>

Considering the effects of COVID-19 on respiratory function are more marked than its cardiovascular impacts,<sup>12</sup> it is unsurprising that most of the studies listed in online supplemental table 1 show respiratory parameters such as RR in CURB-65 to be independently more indicative of mortality than blood pressure and confusion, which are more related to haemodynamics. qSOFA's focus on blood pressure and mental state may explain its lower AUROC and poorer predictive performance. Cetinkal *et al*,<sup>13</sup> however, argue that as previous studies reveal worse clinical outcomes in patients with cardiac injury, non-respiratory variables in the CHA<sub>2</sub>D<sub>2</sub>VASc system such as older age, DM, HTN and previous cardiovascular disease are valuable parameters for mortality risk stratification. However, AUROC values found for CHA<sub>2</sub>D<sub>2</sub>VASc remain at the low end compared with other existing scoring systems, despite modifications catered to COVID-19 added to form the m-CHA<sub>2</sub>D<sub>2</sub>VASc scale. Even this version, with an AUROC higher by 0.06, offers predictive ability similar to univariate NLR and inferior to troponin increase.

Ortiz *et al*<sup>12</sup> demonstrated A-DROP, a modified version of CURB-65, to provide more accurate mortality prediction than *Pneumonia Severity Index* (PSI), CURB-65, CRB-65, SMART-COP, qSOFA and *National Early Warning Score 2* (NEWS2). Its superior discrimination may be due to its more accurate respiratory function evaluation (oxygen saturation [SpO<sub>2</sub>] >90% / arterial oxygen tension [PaO<sub>2</sub>] <60 mm Hg in A-DROP vs respiratory rate ≥30/min in CURB-65). The modified age cut-off (male >70 / female >75 in A-DROP vs age >65 in CURB-65) may also contribute to A-DROP's advantage when applied to COVID-19, considering the median age of COVID-19 non-survivors is 69 years.<sup>14</sup>

Ultimately, although APACHE II, SOFA, PSI and CURB-65 are well-founded in clinical practice, their requirement for sophisticated patient information makes rapid assessment impossible, an important benefit for triaging patients with COVID-19 in often overrun hospitals. Wang *et al*'s study<sup>7</sup> on MEWS suggests this system can overcome the issue of efficiency as a simple and rapid assessment able to be performed within minutes of patient admission while maintaining equal predictive ability.

Intriguingly, Gupta *et al*<sup>15</sup> evaluated 22 prognostic models (including aforementioned systems), concluding that they should not be recommended for routine clinical implementation because none of them offered incremental value compared with univariable predictors to risk stratify COVID-19 mortality, of which patient's age is a strong predictor of mortality. Similarly, Bradley *et al*<sup>16</sup> concluded that CURB-65, NEWS2 and qSOFA all underestimate the mortality of patients with COVID-19.

### COVID-19 scoring systems

To maximise the accuracy and effectiveness of mortality prediction models, novel scores should focus on identifying features that are COVID-19-specific. Examples of complications that are highly associated with COVID-19 include hypercoagulability and inflammation.<sup>17 18</sup> However, only 27% of new prognostic scores included in this review incorporated CRP—an important inflammatory marker. Similarly, thrombopenia has been associated with higher rates of mortality,<sup>19</sup> which reflects the importance of including platelet count in prognostic models, but only 16% of new scores took this into account.

Interestingly, the three prediction models with the highest AUROC values have all used D-dimer and lymphocyte count to predict mortality. This could reflect the importance of these two parameters in COVID-19 pathophysiology. However, these are all single-centre studies tested on significantly smaller sample sizes compared with other models with lower AUROC values. Models tested on a larger population, for instance, Mancilla-Galindo *et al*'s<sup>18</sup> national cohort study with a sample size of 83 779 (AUROC=0.8000), could be more representative and generalisable.

The most common parameter used in novel prediction models for mortality of patients with COVID-19 is age, followed by lymphocyte count, D-dimer, oxygen saturation, CRP and platelet count. Other less common parameters include RR, lactate dehydrogenase, NLR, PCT and blood urea nitrogen.

Fumagalli *et al*<sup>19</sup> report age as the strongest predictor of severe outcomes and mortality. Similarly, Mei *et al*'s<sup>20 21</sup> prognostic model included age as one of five indicators of mortality and reports a strong association between advanced age and death from COVID-19.

There seems to be no association between the number of parameters and the prognostic power and accuracy of a scoring system. Several mortality prediction models with a small number of parameters have had higher AUROC values, for example, Liu *et al*<sup>22</sup> had an AUROC value of 0.9940 with only three variables compared with Mancilla-Galindo *et al*<sup>18</sup> (COVID-GRAM) with an AUROC value of 0.7750 and 10 parameters.

The most common comorbidities for predicting mortality are HTN, DM, obesity, cardiovascular disease, chronic kidney disease, smoking and malignancy.

### Single parameters

COVID-19 has a different clinical picture to pneumonia and influenza, providing an avenue to explore what routinely available clinical information best predicts mortality. We explored blood parameters not currently extensively implemented into existing COVID-19 mortality prediction models, which are represented in online supplemental table 4.

We discuss the feasibility of introducing the below blood tests and imaging modalities into routine practice for risk stratification of patients with COVID-19.

### Cardiac biomarkers

Cardiac biomarkers were the the most common parameters studied in our literature search. High-sensitivity cardiac troponins have been shown to be independently associated with all-cause mortality in patients with COVID-19 ( $p<0.05$ ), after accounting for age, sex and comorbidities, shown in online supplemental table 4. High-sensitivity cardiac troponins (hs-cTnI and hs-TnT) are markers of myocardial injury that are currently primarily used in the prognostication of acute coronary syndrome. Despite evidence that 50% with confirmed COVID-19 have elevated cardiac biomarkers at the time of hospital admission, the patient sample sizes are limited in current studies to less than 500 patients and single centres.<sup>22</sup> Cao *et al*<sup>23</sup> retrospectively observed 244 patients and incorporated hs-cTnI into a model of empirical prognostic factors. A proposed cut-off ( $>20$  ng/L serum hs-cTnI levels) yielded an AUROC increase from 0.65 to 0.71 ( $p<0.01$ ) and demonstrated feasibility of this parameter to increase predictive performance.<sup>24</sup>

### Inflammatory biomarkers

Liu *et al*<sup>25</sup> confirmed the independent association of PCT with mortality in a cohort of 1525 patients through retrospective analysis. Due to the large cohort and continued follow-up of PCT levels throughout hospital stay, this study provides stronger evidence for the inclusion of PCT into scoring systems, which has begun to be implemented but is still in the minority of included parameters. Fois *et al*<sup>26</sup> used the same study design and identified the systemic inflammation index (SII) as an independent predictor of mortality. However, the study quality was poor—with only 119 patients and the large number of different inflammation indexes being studied in different combinations. It is unclear whether any clinical utility is offered by implementation of SSI, considering deranged lymphocyte count is already widely established as a useful predictor.<sup>20</sup>

### Renal and hepatic function biomarkers

Esposito *et al*<sup>27</sup> identified estimated glomerular filtration rate (using a baseline of  $60$  mL/min/ $1.73$  m<sup>2</sup>), and Fu *et al*<sup>24</sup> identified cholestasis and hypoproteinaemia as independent predictors of mortality. Interestingly, as with cardiac biomarkers, these were predictors even after accounting for pre-existing comorbidities. The obvious benefit to clinical practice of renal and hepatic function markers is that they

are routinely done on hospital admission and straightforward to clinicians to score in a system. Replication of large-scale multicentre studies is needed before determining the diagnostic validity of such parameters in the stratification of patients with COVID-19 in a statistical or AI model. It must be acknowledged that additional parameters must be externally validated to determine AUROC values and appropriate cut-offs for parameters.<sup>6</sup>

### Lung imaging

Trabulus *et al*,<sup>28</sup> Francone *et al*<sup>29</sup> and Xu *et al*<sup>30</sup> examined the relationship between chest CT findings and mortality, with all three studies reporting independent associations with mortality ( $p < 0.05$ ). Two studies<sup>31 32</sup> used a methodology involving an overall severity score of each scan and proposed defined cut-offs above which there was yield of best predictive value. These cut-offs are of value for clinicians to allocate scans with a high/medium/low rating which can be used to triage patients with COVID-19. However, both these studies have limitations in their methodology and design, which need to be addressed before implementation of CT severity into scoring systems. In the study by Gao *et al*,<sup>31</sup> follow-up was limited to 24 days; a minimum of at least 28-day mortality is recommended to better reflect the clinical course of COVID-19 in most cases.<sup>7</sup> In addition, both severity score studies were retrospective in nature, which is susceptible to incomplete clinical records and bias in the interpretation of CT by different radiologists. Chest CT while highly sensitive is not a first-line test due to limited resources to CT scan in all COVID-19-positive hospital admissions. Routine implementation of admission CT scans would also carry a radiation burden to patients, which is arguably unnecessary if alternative parameters conferring equal predictive power without additional risk of iatrogenic effects could be used. Perhaps, chest CT is more appropriate in the discharge process of clinically stable, triaged patients with COVID-19 rather than as a first-line test as part of an admission scoring system.

### AI in predicting mortality

Between ML and DL models, it is unclear which branch of AI modelling would be superior in predicting mortality due to the similar AUROC values. These similar values can be accounted for by limitations in the study methods.

Within all AI modelling papers, Meng *et al*<sup>33</sup> and Vaid *et al*<sup>10</sup> were the only studies that conducted external validation. External validation is an important step to verify the effectiveness of the model in patient population. Internal validation would use the same cohort to test the model, which can lead to overfitting and an inaccurately high AUROC. The models created by Bertsimas *et al*<sup>34</sup> Gao *et al*<sup>31</sup> and Meng *et al*<sup>35</sup> gathered training set data from multiple centres, whereas the other models used single-centre data. Therefore, these models would increase applicability to the general population.

As COVID-19 has only been prevalent for a year, not many models have had the chance to be prospectively

tested. Vaid *et al*<sup>10</sup> produced the only model that was prospectively tested. This is important as it demonstrates the model's real-world performance. Many models with a large number of incorporated parameters included patients with missing values, leading to estimation. This may be useful in clinical practice as not all patients have every test carried out.

It is important to recognise that COVID-19 management and treatment guidelines are constantly being updated, which influences mortality rates. As AI models use dynamic data,<sup>10</sup> reporting of model AUROC in earlier stages of the pandemic may not have been as accurate.

### Limitations

There are inherent limitations to this review. Most studies included were single centre and retrospective, whereas multicentre, prospective research may provide more insight. Although AUROC scores are universally accepted outcome measures of the accuracy of prediction models,<sup>6</sup> they are limited in their clinical interpretability as they lack a direct link to individual patient outcomes. Thus, future reviews could use additional performance metrics in addition to AUROC to assess the accuracy of different models.

### CONCLUSION

The above systems and parameters have been evaluated for their ability to stratify patients with COVID-19 by mortality risk, with predictive ability depicted as AUROC scores. New scoring systems developed specifically for the pandemic demonstrated higher AUROC scores than currently existing scoring systems adapted for COVID-19. However, the predictive strength of AI systems was not notably higher than pandemic-specific scoring systems, potentially due to time restraints of development and incomplete refining of algorithms. Single parameters extracted from scoring systems, novel biomarkers and imaging modalities were also explored for the ability to predict mortality and potential incorporation into novel risk stratification systems.

As most studies in the current literature were retrospective, we propose further prospective, multicentre studies to validate these variables' diagnostic accuracy and multivariate relationships, which may impact their compounded efficacy for COVID-19 mortality prediction. A meta-analysis would address the limitation of the current review of not being able to directly compare and statistically manipulate AUROC scores found in the literature due to differing cut-off points, study sample sizes and mortality periods used by different studies.

In all, refining strategies to triage patients with COVID-19 can bring immense value to healthcare professionals in their clinical decisions concerning optimal treatment for patients with varying mortality risks and allocating scarce resources effectively.

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# Call for emergency action to limit global temperature increases, restore biodiversity and protect health

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Wealthy nations must do much more, much faster.

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The United Nations General Assembly in September 2021 will bring countries together at a critical time for marshalling collective action to tackle the global environmental crisis. They will meet again at the biodiversity summit in Kunming, China, and the climate conference (Conference of the Parties (COP)26) in Glasgow, UK. Ahead of these pivotal meetings, we—the editors of health journals worldwide—call for urgent action to keep average global temperature increases below 1.5°C, halt the destruction of nature and protect health.

Health is already being harmed by global temperature increases and the destruction of the natural world, a state of affairs health professionals have been bringing attention to for decades.<sup>1</sup> The science is unequivocal; a global increase of 1.5°C above the pre-industrial average and the continued loss of biodiversity risk catastrophic harm to health that will be impossible to reverse.<sup>2,3</sup> Despite the world's necessary preoccupation with COVID-19, we cannot wait for the pandemic to pass to rapidly reduce emissions.

Reflecting the severity of the moment, this editorial appears in health journals across the world. We are united in recognising that only fundamental and equitable changes to societies will reverse our current trajectory.

The risks to health of increases above 1.5°C are now well established.<sup>2</sup> Indeed, no temperature rise is 'safe'. In the past 20 years, heat-related mortality among people aged over 65 has increased by more than 50%.<sup>4</sup> Higher temperatures have brought

increased dehydration and renal function loss, dermatological malignancies, tropical infections, adverse mental health outcomes, pregnancy complications, allergies, and cardiovascular and pulmonary morbidity and mortality.<sup>5,6</sup> Harms disproportionately affect the most vulnerable, including children, older populations, ethnic minorities, poorer communities and those with underlying health problems.<sup>2,4</sup>

Global heating is also contributing to the decline in global yield potential for major crops, falling by 1.8%–5.6% since 1981; this, together with the effects of extreme weather and soil depletion, is hampering efforts to reduce undernutrition.<sup>4</sup> Thriving ecosystems are essential to human health, and the widespread destruction of nature, including habitats and species, is eroding water and food security and increasing the chance of pandemics.<sup>3,7,8</sup>

The consequences of the environmental crisis fall disproportionately on those countries and communities that have contributed least to the problem and are least able to mitigate the harms. Yet no country, no matter how wealthy, can shield itself from these impacts. Allowing the consequences to fall disproportionately on the most vulnerable will breed more conflict, food insecurity, forced displacement and zoonotic disease, with severe implications for all countries and communities. As with the COVID-19 pandemic, we are globally as strong as our weakest member.

Rises above 1.5°C increase the chance of reaching tipping points in natural systems that could lock the world into an acutely unstable state. This would critically impair our ability to mitigate harms



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and to prevent catastrophic, runaway environmental change.<sup>9 10</sup>

### GLOBAL TARGETS ARE NOT ENOUGH

Encouragingly, many governments, financial institutions and businesses are setting targets to reach net-zero emissions, including targets for 2030. The cost of renewable energy is dropping rapidly. Many countries are aiming to protect at least 30% of the world's land and oceans by 2030.<sup>11</sup>

These promises are not enough. Targets are easy to set and hard to achieve. They are yet to be matched with credible short-term and longer-term plans to accelerate cleaner technologies and transform societies. Emissions reduction plans do not adequately incorporate health considerations.<sup>12</sup> Concern is growing that temperature rises above 1.5°C are beginning to be seen as inevitable, or even acceptable, to powerful members of the global community.<sup>13</sup> Relatedly, current strategies for reducing emissions to net zero by the middle of the century implausibly assume that the world will acquire great capabilities to remove greenhouse gases from the atmosphere.<sup>14 15</sup>

This insufficient action means that temperature increases are likely to be well in excess of 2°C,<sup>16</sup> a catastrophic outcome for health and environmental stability. Critically, the destruction of nature does not have parity of esteem with the climate element of the crisis, and every single global target to restore biodiversity loss by 2020 was missed.<sup>17</sup> This is an overall environmental crisis.<sup>18</sup>

Health professionals are united with environmental scientists, businesses and many others in rejecting that this outcome is inevitable. More can and must be done now—in Glasgow and Kunming—and in the immediate years that follow. We join health professionals worldwide who have already supported calls for rapid action.<sup>19</sup>

Equity must be at the centre of the global response. Contributing a fair share to the global effort means that reduction commitments must account for the cumulative, historical contribution each country has made to emissions, as well as its current emissions and capacity to respond. Wealthier countries will have to cut emissions more quickly, making reductions by 2030 beyond those currently proposed<sup>20 21</sup> and reaching net-zero emissions before 2050. Similar targets and emergency action are needed for biodiversity loss and the wider destruction of the natural world.

To achieve these targets, governments must make fundamental changes to how our societies and economies are organised and how we live. The current strategy of encouraging markets to swap dirty for cleaner technologies is not enough. Governments must intervene to support the redesign of transport systems, cities, production and distribution of food, markets for financial investments, health systems, and much more. Global coordination is needed to ensure

that the rush for cleaner technologies does not come at the cost of more environmental destruction and human exploitation.

Many governments met the threat of the COVID-19 pandemic with unprecedented funding. The environmental crisis demands a similar emergency response. Huge investment will be needed, beyond what is being considered or delivered anywhere in the world. But such investments will produce huge positive health and economic outcomes. These include high-quality jobs, reduced air pollution, increased physical activity, and improved housing and diet. Better air quality alone would realise health benefits that easily offset the global costs of emissions reductions.<sup>22</sup>

These measures will also improve the social and economic determinants of health, the poor state of which may have made populations more vulnerable to the COVID-19 pandemic.<sup>23</sup> But the changes cannot be achieved through a return to damaging austerity policies or the continuation of the large inequalities of wealth and power within and between countries.

### COOPERATION HINGES ON WEALTHY NATIONS DOING MORE

In particular, countries that have disproportionately created the environmental crisis must do more to support low-income and middle-income countries to build cleaner, healthier and more resilient societies. High-income countries must meet and go beyond their outstanding commitment to provide \$100 billion a year, making up for any shortfall in 2020 and increasing contributions to and beyond 2025. Funding must be equally split between mitigation and adaptation, including improving the resilience of health systems.

Financing should be through grants rather than loans, building local capabilities and truly empowering communities, and should come alongside forgiving large debts, which constrain the agency of so many low-income countries. Additional funding must be marshalled to compensate for inevitable loss and damage caused by the consequences of the environmental crisis.

As health professionals, we must do all we can to aid the transition to a sustainable, fairer, resilient and healthier world. Alongside acting to reduce the harm from the environmental crisis, we should proactively contribute to global prevention of further damage and action on the root causes of the crisis. We must hold global leaders to account and continue to educate others about the health risks of the crisis. We must join in the work to achieve environmentally sustainable health systems before 2040, recognising that this will mean changing clinical practice. Health institutions have already divested more than \$42 billion of assets from fossil fuels; others should join them.<sup>4</sup>

The greatest threat to global public health is the continued failure of world leaders to keep the global temperature rise below 1.5°C and to restore nature.

Urgent, society-wide changes must be made and will lead to a fairer and healthier world. We, as editors of health journals, call for governments and other leaders to act, marking 2021 as the year that the world finally changes course.

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