phenotypes despite significant differences in the population that it was tested on and the population the model was derived from. Although these markers cannot be easily quantified in clinical practice and prospective validation is still required, using this simple algorithm in a trial setting will improve the ability to target interventions in groups at increased chance of benefit.

PREDICTION MODELS FOR SEVERITY OF COVID-19 INFECTION: PLENTY OF DATA BUT MORE NEEDED

The COVID-19 pandemic is putting a strain on healthcare systems globally. Prediction models can assist in triaging patients and resource allocation. Wynants *et al* (*BMJ* 2020; 369:m1328) performed a systematic review of available prediction models for COVID-19 infections in collaboration with the Cochrane Prognosis Methods Group. An initial search retrieved 2696 titles producing 27 studies, describing 31 models of which all but one used clinical data from within China. Using established protocol for systematic review analysis, the authors sought to extract each model's predictive performance through reported discrimination (C index) and calibration (intercept and slope) as reported by TRIPOD (Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis). None seems to be ready for use in clinical practice reliably; models aiming to predict diagnosis on suspected cases did not adequately assess calibration, which makes them unreliable, despite excellent predictive performance with C indices of 0.87–0.98. Prognostic models showed significant variation, with mortality risks of 8%–59%. Only two prognostic model studies reported a C index and only one reported calibration; however, when applied to new patients, the probabilities of mortality were too low for high-risk patients and too high for low-risk patients (calibration slope > 1). Despite the large number of studies, there remains a lack of robust data to support clinicians with a lack of well-developed models.

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REMEDESIVIR FOR PATIENTS WITH SEVERE COVID-19: A POSSIBLE THERAPEUTIC OPTION?

Currently, there are no effective antiviral treatments for COVID-19, and given the impact of the global pandemic urgent attempts are being made to develop potential therapies. Grein *et al* (*N Engl J Med* 2020, doi: 10.1056/NEJMoa2007016) performed an open-label prospective cohort study of 53 patients who were granted compassionate use of remdesivir (a prodrug of a nucleoside analogue that inhibits viral RNA polymerases). The duration of treatment was set as 10 days, with a follow-up period of 28 days (median 18; IQR 13–23). The cohort was 75% male with a median age of 64 (48–71) years and a median time of 2 (1–8) days on invasive ventilation prior to initiation of remdesivir. The authors measured the incidence of what they defined as key events: changes in oxygen support requirements, hospital discharge, adverse events and death. There were no predefined endpoints. All patients had confirmed COVID-19 via reverse transcriptase-PCR assay. The trial-defined clinical improvement occurred in 68% (36 of 53) of all patients and was less likely in patients receiving invasive ventilation (HR 0.33, 95%CI 0.16 to 0.68) and those >70 years old (compared with patients <50 years old; HR 0.29, 95%CI 0.11 to 0.74). Overall mortality was 13%, which compares favourably with contemporaneous cohorts. There were no major safety concerns during the trial. No definite conclusions can be extrapolated from this study regarding remdesivir use given the design, small sample size and several bias risks. A large randomised controlled trial will hopefully shed some more light regarding its efficacy.

COVID-19 PNEUMONIA: PREDICTING THOSE AT RISK OF ARDS AND DEATH

Early identification of patients at risk of deteriorating is important in guiding their treatment as well as in the effort to distribute resources. Wu *et al* (*JAMA Intern Med* 2020, doi: 10.1001/jamainternmed.2020.0994) explored whether epidemiological and clinical features in patients with COVID-19 are associated with progression to acute respiratory distress syndrome

(ARDS) and/or death. They looked retrospectively at 201 patient records; 84 developed ARDS (41.8%), 53 (26.4%) required admission to the intensive care unit and 44 died (21.9%). All patients who died had developed ARDS and required mechanical ventilation. Clinical features including age (difference between patients without and with ARDS (Δ) 12.0 years; 95%CI 8.0 to 16.0, $p<0.001$), hypertension (Δ 13.7%; 95%CI 1.3% to 26.1%, $p=0.02$) and diabetes (Δ 13.9%; 95%CI 3.6% to 24.2%, $p=0.002$) increased the risk of ARDS. Laboratory tests including elevated D-dimer (Δ 0.52 $\mu\text{g/mL}$; 95%CI 0.21 to 0.94 $\mu\text{g/mL}$, $p<0.001$) and lymphopaenia ($-0.34\times 10^9/\text{mL}$; 95%CI -0.47 to $0.22\times 10^9/\text{mL}$, $p<0.001$) were also associated with ARDS. Within the ARDS subgroup, not all the above were necessarily associated with progression to death. Older age, neutrophilia, and organ and clotting dysfunction were the strongest risk factors for dying. Within the limitations of a single-centre study, clinicians can use these data to support decision making for allocation of treatment in hospitalised patients with COVID-19 infection.

NEW TOOLS FROM OLD DATA: IDENTIFYING SUBGROUPS OF ARDS

The broad clinical definition and heterogeneity of acute respiratory distress syndrome (ARDS) have contributed to the limited success of interventions in clinical trials. Sinha *et al* (*Lancet Respir Med* 2020, 8:247) performed a secondary analysis of randomised control trial cohorts to develop an easy-to-use algorithm aiming to identify ARDS subgroups. Previous work identified hypoinflammatory and hyper-inflammatory groups via latent class analysis (LCA) with distinct biological and clinical features including differences in mortality and duration of ventilation. They built their model using LCA-derived phenotypes as the reference standard from a derivation data set ($n=2022$) and then used machine-learning algorithms and logistic regression to select a maximum of six important variables. In comparison, LCA uses up to 40 variables. When testing their models on an out-of-sample validation data set ($n=715$), they concluded that a three-variable model balanced classifying accuracy and model simplicity (AUC 0.94, 95% CI 0.92 to 0.95). The variables selected were interleukin-8, bicarbonate and protein C. At a probability cut-off to assign phenotype of 0.5, specificity was 0.95 and sensitivity was 0.74. During external validation, the results of the three-variable model were comparable with LCA-derived

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