suggests a complex set of immunological,[2,3] platelet, and endothelial abnormalities,[4] possibly linked to viral persistence.[5] Testing antihistamine response and being aware of potential dietary triggers are simple, low-risk interventions that have support from clinicians treating patients with long COVID. A clinical trial of antihistamines, led by University College London Hospitals, is about to start (STIMULATE-ICP), but will be over a year in reporting. We do not consider that mast cell disorder is the cause of long COVID, but a potential symptom target, alongside postural orthostatic tachycardia syndrome, and treating either or both if present is something that GPs can offer now to help many patients with long COVID.

Brendan C Delaney,

GP and Chair in Medical Informatics and Decision Making, Imperial College London, London.
Email: brendan.delaney@imperial.ac.uk

Clare Rayner,

Occupational Physician, Independent.

Anette Freyer,

Consultant in Acute and Obstetric Medicine, Nottingham University Hospitals NHS Trust, Queen's Medical Centre, Nottingham.

Sharon Taylor,

Consultant Child And Adolescent Psychiatrist, Central and North West London NHS Foundation Trust, London.

Linn Järte,

CT2 Anaesthetist, Anaesthetics Department, Morriston Hospital, Swansea Bay University Health Board, Swansea.

Nathalie MacDermott,

NIHR Academic Clinical Lecturer, St Mary's Hospital, Imperial College NHS Trust, London.

Martine Nurek,

Postdoctoral Research Associate, Department of Surgery and Cancer, Imperial College London, London.

REFERENCES

1. Office for National Statistics. *Prevalence of ongoing symptoms following coronavirus (COVID-19) infection in the UK.* 2022. https://tinyurl.com/3dsw7mnz (accessed 10 May 2022).
2. Weinstock LB, Brook JB, Walters AS, *et al.* Mast cell activation symptoms are prevalent in Long-COVID. *Int J Infect Dis* 2021; **112:** 217–226.
3. Kell DB, Laubscher GJ, Pretorius E. A central role for amyloid fibrin microclots in long COVID/PASC: origins and therapeutic implications. *Biochem J* 2022; **479(4):** 537–559.
4. Oikonomou E, Souvaliotis N, Lampsas S, *et al.* Endothelial dysfunction in acute and long standing COVID–19: a prospective cohort study. *Vascul Pharmacol* 2022; **144:** 106975.
5. Proal AD, VanElzakker MB. Long COVID or post-acute sequelae of COVID-19 (PASC): an overview of biological factors that may contribute to persistent symptoms. *Front Microbiol* 2021; **12:** 698169.

DOI: https://doi.org/10.3399/bjgp22X719549

Development and external validation of a new clinical prediction model for early recognition of sepsis

The inclusion of criteria selected only the sickest of patients in the article by Loots *et al*,[1] with 42% ultimately being diagnosed with sepsis. The inclusion criteria were: *'Acutely ill adult (≥18 years) patients with fever, confusion, general deterioration, or otherwise suspected severe infection were eligible for inclusion.'* The exclusion of respiratory rate as *'less feasible for GPs to perform'* merits further consideration of the wider implications.

The title of this article may be misleading: the presumptive diagnosis of sepsis in a confused, feverish adult with *'suspected severe infection'* is not an 'early' diagnosis. The title might be amended to *'... a new clinical prediction model for accurate recognition of sepsis in housebound seriously ill adults'*. The applicability and validity of this scoring model in 'routine GP out-of-hours' is unproven.

Diarmuid Quinlan,

GP, Irish College of General Practitioners.
Email: drdiarmuidquinlan@hotmail.com

REFERENCE

1. Loots FJ, Smits M, Hopstaken RM, *et al.* New clinical prediction model for early recognition of sepsis in adult primary care patients: a prospective diagnostic cohort study of development and external validation. *Br J Gen Pract* 2022; DOI: https://doi.org/10.3399/BJGP.2021.0520.

DOI: https://doi.org/10.3399/bjgp22X719561

Author response

We thank Diarmuid Quinlan for the interest in our study, and he correctly points out that the patients included in the study have a substantially higher risk compared with the average adult patient assessed by a GP. We do not advocate to use the new derived model to screen for sepsis in all adult patients with a suspected infection presenting in primary care, as this would unnecessarily increase the workload for GPs and result in many false-positive cases. In our view, a predictive model should be used only in cases where a GP perceives a clinical problem. Therefore, we decided to include only study subjects with relevant signs and/or symptoms and those in whom the GP suspected a serious infection. This however did not lead to a study population with *'only the sickest of patients'*. The proportion of patients meeting the Sepsis-3[1] criteria was high (42%), but this does not mean all patients were critically ill at the time of inclusion. The rate of referral to the hospital after the index consultation was 56%, and 3% of the patients were admitted to the ICU.

We do not feel the phrasing *'early recognition of sepsis'* in the title is misleading. The population included in the study is a high-risk population for sepsis, but we included patients directly after the first contact with the out-of-hours GP cooperative and almost half of the patients were not referred to the hospital after inclusion. We expect the model to be valid for all patients suspected of sepsis or otherwise having signs of a serious infection in the primary care setting, but, as we stated in the article, additional research is needed before widely adopting the model in practice.

Feike Loots, on behalf of the co-authors,

PhD Candidate, Julius Center for Health Sciences and Primary Care, University Medical Centre Utrecht, Utrecht University, Utrecht.
Email: f.j.loots@umcutrecht.nl

REFERENCE

1. Singer M, Deutschman CS, Seymour CW, *et al.* The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA* 2016; **315(8):** 801–810.

DOI: https://doi.org/10.3399/bjgp22X719573