



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Reaffirming health and safety precautionary principles for COVID-19 in the UK

In their case for a sustainable UK strategy for COVID-19, Deepti Gurdasani and colleagues¹ recommend "restoration of an adequate health and safety inspectorate". We do not believe that the UK Health and Safety Executive (HSE) should, like Public Health England, be made a scapegoat for lack of ministerial direction² but rather that the HSE should be restored the wherewithal to fulfil its mandate.

The HSE needs to step up in this pandemic, independently of political influence, and to firmly enforce occupational hygiene measures for source control, including regular staff testing, segregation, and ventilation.² Moreover, the HSE should apply precautionary principles with regards to the proliferating evidence for aerosol transmission of severe acute respiratory syndrome coronavirus 2.³

The HSE should recognise research, such as its own showing the marked superiority of filtering facepiece respirators (eg, FFP3) over surgical masks,² and should re-assert its own guidance⁴ to use such respirators as personal protective equipment (PPE) for workers.

Early in the pandemic, the HSE adopted a risk-adapted management strategy⁵ and tolerated less stringent PPE requirements, perhaps because of the inadequate, depleted, and neglected state of the national stockpile of PPE.² Several months have since elapsed, and billions of pounds of taxpayers' money has been spent amassing huge stocks of PPE. It is not clear why the HSE is still not recommending respirators as PPE for public transport workers and other public-facing occupations, as well as in health and social care in situations where control at source, barriers, and ventilation are not adequate.

We declare no competing interests.

*Raymond M Agius, Denise Kendrick, Herb F Sewell, Marcia Stewart, John FR Robertson
rmagius@doctors.org.uk

University of Manchester, Manchester M13 9PL, UK (RMA); University of Nottingham, Nottingham, UK (DK, HFS, JFRR); De Montfort University, Leicester, UK (MS)

- 1 Gurdasani D, Bear L, Bogaert D, et al. The UK needs a sustainable strategy for COVID-19. *Lancet* 2020; **396**: 1800–01.
- 2 Agius RM. COVID-19 and health at work. *Occup Med (Lond)* 2020; **70**: 349–51.
- 3 Agius RM, Robertson JFR, Kendrick D, Sewell HF, Stewart M, McKee M. COVID-19 in the workplace. *BMJ* 2020; **370**: m3577.
- 4 Health and Safety Executive. Respiratory protective equipment at work. A practical guide. HSG53, 4th edn. Bootle: Health and Safety Executive, 2013. <https://www.hse.gov.uk/pubns/books/hsg53.htm> (accessed Jan 12, 2021).
- 5 Robertson JFR, Stewart M, Kendrick D, Sewell HF. COVID-19: protect health and social care workers and refer their deaths to the coroner. April 21, 2020. <https://blogs.bmj.com/bmj/2020/04/21/covid-19-protect-health-and-social-care-workers-and-refer-their-deaths-to-the-corerone/> (accessed Jan 8, 2021).

Considering dose in pharmacological therapies for heart failure

Muthiah Vaduganathan and colleagues¹ analysis was insightful in contextualising the potential benefits observed in trials for the medical treatment of heart failure with reduced ejection fraction (HFrEF). A noted shortcoming of the analysis was not accounting for the role of the dose of disease-modifying medication in the disease course of HFrEF. Vaduganathan and colleagues¹ correctly identified the CHAMP-HF,² QUALIFY,³ and CHECK-HF⁴ registries as evidence of the underuse of mineralocorticoid receptor antagonists (MRAs) and angiotensin receptor neprilysin inhibitors, but they also attributed the stagnation in HFrEF mortality to this underuse. However, the prevalent underdosing of β blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and MRAs on a population level was just as important a finding in these studies. Underdosing

can be identified as an equally, if not more, important driver of mortality in patients with HFrEF.

Major cardiology societies recommend titration to target doses of referenced disease-modifying medications because these doses have an established mortality benefit in large randomised controlled trials. Importantly, the inclusion criteria for the DAPA-HF⁵ and PARADIGM-HF⁶ trials did not control for β blocker dose, and consequently the analysis by Vaduganathan and colleagues¹ also did not.

By ignoring the effect of dosing, the analysis did not acknowledge the possibility of dose-dependent medication interactions between conventional and comprehensive medication groups. For example, the extent to which the adequate titration of β blockers and MRAs impacts the beneficial or adverse effects observed with the addition of sacubitril valsartan and dapagliflozin is unknown. This knowledge gap is particularly important because the exact mechanism by which inhibition of SGLT2 improves outcomes in patients with HFrEF remains uncertain.

Admittedly, given the variability in dosing practices, producing a similar analysis that accounts for dose would be difficult. Regardless, disclosing this confounding factor is still essential.

We declare no competing interests.

Zed Seedat, *Kevin Itty
kitty@health.fau.edu

Department of Integrated Medical Sciences, Florida Atlantic University, Boca Raton, FL 33431, USA

- 1 Vaduganathan M, Claggett BL, Jhund PS, et al. Estimating lifetime benefits of comprehensive disease-modifying pharmacological therapies in patients with heart failure with reduced ejection fraction: a comparative analysis of three randomised controlled trials. *Lancet* 2020; **396**: 121–28.
- 2 Greene SJ, Butler J, Albert NM, et al. Medical therapy for heart failure with reduced ejection fraction: the CHAMP-HF registry. *J Am Coll Cardiol* 2018; **72**: 351–66.
- 3 Komajda M, Schöpe J, Wagenpfeil S, et al. Physicians' guideline adherence is associated with long-term heart failure mortality in outpatients with heart failure with reduced ejection fraction: the QUALIFY international registry. *Eur J Heart Fail* 2019; **21**: 921–29.