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.

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Authors' reply

We thank Nicholas Wald and colleagues for their interest in our work.[1] They propose that our findings merely confirmed what has been previously known, as reported by them.

We summarised[1] relevant previous research and the evidence gap around the effects of blood pressure reduction in the very young and the very old, and whether the recommended use of age-dependent blood pressure thresholds for inititation or intensification of treatment by some clinical practice guidelines[2,3] are justified. Wald and colleagues' work was very valuable but did not investigate these particular questions, and we could therefore neither confirm nor refute their findings. We reviewed and cited other meta-analyses that attempted to investigate these questions, and we discuss the novelty and added value of our work to clinical decision making in their context.

In comparison with earlier reports, our meta-analysis benefited from access to the largest source of individual participant-level data.[4,5] This meant that we were able to simultaneously stratify effects by age (in 10-year increments from age <55 years to ≥85 years) and blood pressure (in 10 mm Hg increments from <120 mm Hg to ≥170 mm Hg systolic, and from <70 mm Hg to ≥110 mm Hg diastolic) at baseline, while standardising for differing intensities of blood pressure reduction in individual trials. No meta-analysis has previously provided this level of detail. This advantage is analogous to looking at a dataset through a microscope; the higher resolution analysis helps reveal previously hidden relationships (even if theoretically assumed by some). For instance, although beneficial effects in lowering cardiovascular events were seen in most age groups (and blood pressure levels), the relative risk reductions per 5 mm Hg reduction in systolic blood pressure appeared to diminish with age and in people aged 85 years or older, the effect was highly uncertain (hazard ratio 0·99, 95% CI 0·87–1·12). These results do not seem to support Wald and colleagues' generalisation that any aged 50 years or older stands to benefit similarly from blood pressure-lowering treatment.

We do not dispute the need for better solutions that help overcome the implementation gap, as Wald and colleagues have suggested. However, providing reliable and precise quantification of expected treatment effects in a wide range of at-risk groups,[1] as we have done, is an important and necessary step towards informing better decisions and addressing those implementation gaps.

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An open letter to the Executive Board of WHO from the surgical and anaesthesia community

An estimated 28 million surgeries were cancelled worldwide during the first 3 months of the COVID-19 pandemic, a number which might now be as high as 115 million—more than a third of all surgeries annually.[1,2] We applaud the work of WHO over the past 2 years in managing and reducing the impacts of the pandemic, but are critical about the efforts taken to mitigate the impact of cancelled surgeries despite the recognition of surgery as an essential part of universal health coverage. Given the unequal impacts the pandemic has had across clinical disciplines, countries, and populations, we strongly support the development of a binding worldwide pandemic treaty.

With the sharp rise in non-communicable diseases worldwide, the demand for surgical care is rapidly increasing. Surgical interventions are needed for 80% of injured patients and more than half of patients with cancer.[3] Given the high versatility and the clear value surgical teams and infrastructure have added to the pandemic response, it is surprising that surgical system strengthening has not received more attention as part of pandemic preparedness initiatives thus far. We suggest a paradigm shift where access to surgical care is mainstreamed into pandemic preparedness policies. A mainstreaming approach would entail that the pandemic treaty assures that every policy adopted or implemented from this treaty has been evaluated for its impact on national-level surgical care provision. Only policies that do not harm surgical care provision should be included in the final version of the treaty so as to avoid detrimental impact. While novel in global surgery discourse, this would entail a policy approach similar to WHO's Health in All Policies.

As defined by the UN General Assembly at the beginning of the pandemic, this approach involves considering the systemic impact of policy decisions on health and making those decisions across different sectors to achieve synergy, equity, and improved health outcomes.[4] By mainstreaming surgery into pandemic preparedness policy, we suggest that surgical care provision is taken into consideration for every policy recommendation or operative paragraph. This way, true health systems strengthening can take place to achieve a system where no-one is left behind before, during, or after a pandemic.

The 150th WHO Executive Board established a Standing Committee on Pandemic and Emergency Preparedness and Response to draft and negotiate the Pandemic Treaty under the sole auspices of the Member States.[5] We urge the committee to recognise the importance of surgery as an essential part of health systems by: (1) ensuring participation of civil society, including the surgical community, as key stakeholders in the treaty negotiation process; and (2) mainstreaming surgical care into the final draft of the Pandemic Preparedness Treaty.

The surgical and anaesthesia communities stand ready to be involved in this process.

We declare no competing interests. Signatories of this Correspondence are listed in the appendix.

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Host-targeting oral antiviral drugs to prevent pandemics

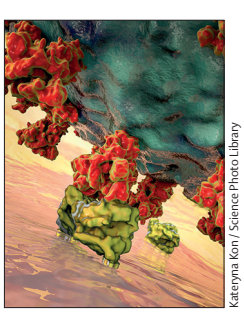
Unlike bacteria, viruses must use host cells to replicate. This has enabled us to identify the Achilles heel of many viruses. We want to exploit this knowledge for the therapeutic targeting of current major human pathogens, such as coronaviruses and influenza for which there is a great unmet need. The orally available small molecule broad-spectrum antiviral compounds we have developed over many years target the host[1] and are thus resistant to viral mutations. Host-targeting drugs can also be employed against newly emerging viruses even before detailed information about the virus becomes available.[2,3] This will be crucial in preventing the inevitable new epidemics from turning into pandemics.

Most enveloped viruses need to use a sugar-mediated pathway in the infected human host cell to form their correct three-dimensional structures, which involves adding and processing glycans on viral envelope glycoproteins.[2,3] The glycosylation process involves enzymes in the cell trimming the sugars of the viral glycoproteins for entry into this protein folding quality control pathway. Drugs that partially inhibit these enzymes prevent the virus from making proper use of this folding pathway and lead to inhibition of secretion of infectious virus.[4–8]

Over the past 25 years, we have developed a class of drugs called iminosugars—orally available sugar mimetics that are recognised by and inhibit these sugar processing enzymes that most enveloped viruses rely on.[1] The family of iminosugars derive from the parent compound initially isolated from the leaves of the mulberry tree.

Safety and efficacy data in animals accumulated over the past 20 years show that iminosugar derivatives reduce viral levels and increase survival in animal models of chronic hepatitis B infection,[6] hepatitis C, Japanese encephalitis, influenza,[9] and dengue.[7,8] When tested in vitro against over 31 clinical HIV isolates, including HIV-1, HIV-2, and multidrug resistant strains, iminosugars are active against a diverse panel of HIV-1 from different genetic subtypes and geographical regions, and against HIV-2 isolates and mutants resistant to antiretrovirals.[10] All HIV isolates tested were rendered non-infectious by iminosugar treatment. Similarly,

See Online for appendix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