COVID-19 testing delays and pathology services in the UK

Richard Horton[1] is critical of the UK Government for not following WHO's advice for COVID-19 testing at a much earlier stage of the pandemic and for not securing supply chains for pharmaceuticals, protective equipment, and appropriate human resources.

Following the 2003 severe acute respiratory syndrome outbreak and the 2012 Middle East respiratory syndrome outbreak, it was inevitable that with global population growth, overcrowding in many low-income and middle-income countries, increased cheap air travel, and failure to stamp out wet and live animal markets, new coronaviruses would emerge and spread rapidly. The UK should have prioritised the development and availability of better technology to detect new viruses and manage their spread.

10 years of austerity have left the UK National Health Service inadequately resourced and ill prepared. During the reorganisation of pathology services, recommended by the 2008 Carter report,[2] many hospital laboratories have disappeared with the introduction of so-called hub and spoke models. This has been at the expense of what had previously been a high-quality service for diagnosis, surveillance, and epidemiology. Furthermore, there has been a failure to stockpile laboratory consumables and reagents, despite shortages during the 2009 H1N1 influenza pandemic.[3] What is particularly inexcusable is the shortage of swabs to take samples from patients and health-care workers during the current COVID-19 pandemic. Our reliance on China as a global supplier for such supplies has compromised the UK's COVID-19 response. Many manufacturers, suppliers, and hospital services are inevitably finding it difficult to meet the demand for testing of both patients and staff.

The centralisation of pathology services into a hub and spoke model has resulted in the hub being located at a site distant to some acute services. The reduction in the number of senior scientific staff to reduce costs has failed to increase enthusiasm for what should be an exciting and attractive career for both doctors and scientists. The geographical and intellectual separation of service and academic activities precludes an interactive approach to diagnosis, management, and research. In many medical schools, there has been a reduction in pathology teaching in the undergraduate curriculum, such that students are not interested in some of the major developments in medicine.

The Royal College of Pathologists and the other pathological societies should be more vocal in recognising the importance of their disciplines. It is disappointing that other specialties that are dependent on pathology have not spoken up to express their views at a local or national level in the face of damaging reorganisation and cuts in pathology.

In short, the disciplines that manage infections, microbiology, and virology, have been undervalued and underresourced for a long time. Only if things change will we be able to improve responses to new infections.

I declare no competing interests.

Jangu Banatvala
jangu.banatvala@gmail.com

School of Medicine and Dentistry, Kings College London, London WC2R 2LS, UK

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Questioning statin therapy for older patients

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Single clinical trials have not yet determined whether statin therapy provides more benefit than harm to people older than 75 years with or without a history of vascular disease. The Cholesterol Treatment Trialists' Collaboration, which alone has access to patient-level data from most trials, is best able to answer these questions. However, we have several concerns about the Article by the Collaboration[1] and the presentation of its results to the media.

First, the collaboration states that "rates of use of statin therapy… are substantially lower in people older than 75 years",[1] but the data in table 2 of one of the two sources cited to support this claim, by Salami and colleagues,[2] show just the opposite.

Second, although the collaboration reports that they have data on 14 483 trial participants older than 75 years, approximating the total denominator of all such participants from the figures in the 2019 meta-analysis gives only 9473 participants for figure 1A and 10 513 participants for figure 5A (by dividing the number of events by % per annum ÷ 100 × median number of years per study). Thus, either the collaborations' calculations are missing 27–35% of the available data or a considerable number of trials had short follow-ups. Although short follow-ups would explain this discrepancy through a difference between the median and mean duration of the studies, we find this explanation untenable because of the magnitude of the difference; it is at least worthy of additional explanation.

Third, the collaboration's data show that annually, 1000 people older than 75 years without a history of vascular disease need treatment to prevent a single major vascular event, and cardiovascular or all-cause mortality data are not presented for this population. These results make informed doctor–patient decisions

impossible, especially when the frequency of side-effects that are meaningful to patients is simply not known.

Because most people older than 75 years do not have vascular disease[3] and the Collaboration does not present mortality data for this population, we believe the Collaboration was irresponsible in relaying to the media that 8000 deaths could be prevented each year if all UK citizens aged 75 years or older took statins.[4]

Given these gaps in the data, we believe it is wrong to recommend statin therapy uniformly for people aged 75 or older who do not have cardiovascular disease. A far more beneficial public health message is the strong evidence for the cardiovascular benefit of maintaining a healthy lifestyle, especially including routine exercise.

Finally, doctors and patients need to be reminded that patient-level data held by the Collaboration remain unavailable for independent analysis and therefore have not been verified.

For more on the **Cholesterol Treatment Trialists' Collaboration** see https://www.cttcollaboration.org/about2

For more on the **Independent Oversight Panel** see https://www.cttcollaboration.org/independent-oversight

JA has served as an expert for plaintiffs' attorneys in litigation involving Avandia and Crestor, and is writing a book about the pharmaceutical industry. NJ has served as an expert for the defence attorneys in litigation involving Ferrirprox and Aranesp, and for the plaintiffs' attorneys in litigation involving Neratinib, Loestrin 24 Fe, Suboxone, Doryx, Zoloft, Prozac, Lipitor, and Granuflo. All other authors declare no competing interests.

*John Abramson, Curt Furberg, Nicholas Jewell, James M Wright
john_abramson@hms.harvard.edu

Harvard Medical School, Health Care Policy, Boston, MA 02115, USA (JA); Division of Public Health Services, Wake Forest University, Winston-Salem, NC, USA (CF); Department of Medical Statistics, London School of Hygiene & Tropical Medicine, London, UK (NJ); and Department of Anesthesiology, Pharmacology and Therapeutics (JMW) and Department of Medicine (JMW), University of British Columbia, Vancouver, BC, Canada

1 Cholesterol Treatment Trialists' Collaboration. Efficacy and safety of statin therapy in older people: a meta-analysis of individual participant data from 28 randomised controlled trials. *Lancet,* 2019; **393:** 407–15.
2 Salami JA, Warraich H, Valero-Elizondo J, et al. National trends in statin use and expenditures in the US adult population from 2002 to 2013: insights from the Medical Expenditure Panel Survey. *JAMA Cardiol* 2017; **2:** 56–65.
3 Johansen ME, Green LA. Statin use in very elderly individuals, 1999–2012. *JAMA Int Med* 2015; **175:** 1715–16
4 Torjesen I. GPs should consider offering statins to all patients aged over 75, researchers say. *BMJ* 2019; **364:** 1522.

Authors' reply

We were correct in stating that, among patients with established cardiovascular disease, the rates of use of statin therapy have been shown to decline among people older than 75 years.[1] Not only do the Dutch data[2] that we cited demonstrate this trend, but so do the US data reported by Salami and colleagues.[3] Supplementary table 5a in the latter paper[3] indicates that, after adjusting for other factors, the odds of statin use among patients with cardiovascular disease are about one-fifth lower among patients aged 75 or older than among patients aged 65–74 years.

Data on individual participants in randomised trials of statin therapy were made available to the Cholesterol Treatment Trialists' Collaboration on the basis that they would not be shared with third parties. However, an independent panel provides external oversight, and the Collaboration responds to external requests for analyses. Additional information is included in online appendices to published reports; for example, table 1 in the online appendix to our Article[1] documents that 14 483 patients older than 75 years contributed to the meta-analyses (avoiding the need for estimation).

Combined analyses of the primary and secondary populations in these statin trials indicate that the proportional reductions in major vascular events and vascular deaths are similar irrespective of age. Consequently, as discussed in our Article[1] and elsewhere,[4] the absolute benefits of statin therapy can be estimated by applying the overall proportional reduction in major vascular events of about a fifth per mmol/L reduction in LDL cholesterol to the absolute risk among people at different ages (rather than by applying risk reductions observed in individual age groups). That approach was also used to estimate that wider use of statins in the UK among people older than 75 years might prevent up to 8000 deaths annually, as well as larger numbers of non-fatal heart attacks and ischaemic strokes.

The example provided in our Article[1] compared two individuals in a primary prevention setting, aged 63 years and 78 years, with otherwise identical risk factors. The projected annual vascular event risk was 2·5% for the patient aged 63 years and 4·0% for the patient aged 78 years. Reducing their risk by a fifth by lowering LDL cholesterol by 1 mmol/L would prevent major vascular events from occurring in 50 of 10 000 patients during each year of treatment for patients aged 63 years, and in 80 of 10 000 people during each year of treatment in patients aged 78 years. This reduction would translate into a number needed to treat (NNT) per year of less than 200 in both cases. Even larger risk reductions (and lower NNTs) would be expected with larger LDL cholesterol reductions.[4] Direct evidence of the effects of statin therapy in the primary prevention setting among patients aged over 75 years is in short supply, but such evidence will be provided by ongoing randomised trials.

We agree that it is appropriate to emphasise the benefits of a healthy lifestyle, but this should be in addition to (not instead of) consideration of the wider use of statins in older people whose healthy lives might be ended by disabling heart attacks or strokes that could have been avoided. Moreover, it is important that the incidence of side-effects attributed to statin therapy is not exaggerated, since misinformation has been shown to cause substantial harm to the public.[4]

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