

the establishment and operation of data and safety monitoring boards.

We are scientists, physicians, funders, and policy makers who have come together in an international coalition, the COVID-19 Clinical Research Coalition, to support WHO's efforts to counter the COVID-19 pandemic. We commit our combined experience, expertise, and trial capability to accelerate COVID-19 research in resource-limited settings. We welcome collaboration with organisations ready to contribute existing capacity to join us at the website of the COVID-19 Clinical Research Coalition.

MEB and PH are principal investigators or co-investigators in multiple vaccine development programmes, including for SARS, Middle East respiratory syndrome, and COVID-19 and have grants from the US National Institutes of Health (NIH), for research towards the development of COVID-19 vaccine. PC reports grants from Merck and ViiV Healthcare. SC has a patent PCT/IB2011/055209 with royalties paid to Nearmedic Plus for a tuberculosis drug candidate. JF is Director of the Wellcome Trust. AG receives non-financial support from University of Nairobi. DR reports grants from the Bill & Melinda Gates Foundation, the Wellcome Trust, the Governments of Australia, Ireland, Germany, Monaco, Netherlands, Switzerland, Korea, the UK, and the USA, GHIT Japan, EDCTP, UNITAID, and WHO. MT reports personal fees for board membership from Fondation Botnar (not-for-profit), personal fees for member of scientific advisory board from Novartis Institute for Tropical Diseases, personal fees for board membership from Gebert-Rüf Foundation (not-for-profit), personal fees for board chair from R Geigy Foundation (not-for-profit), personal fees for board membership from University Hospital Basel, Switzerland (public hospital), and personal fees for member of University Senate from the University of Neuchatel (public institution). We declare no other competing interests.

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For the COVID-19 Clinical Research Coalition see [www.covid19crc.org](http://www.covid19crc.org)

See Online for appendix



## An alarming rise in incidence of infective endocarditis in England since 2009: why?

Infective endocarditis is a life-threatening condition with a 50% requirement for early cardiac surgery and 30% mortality at 1 year.<sup>1</sup> We have used publicly available annual admission data for hospitals in England<sup>2</sup> to examine the incidence of infective endocarditis admissions (primary ICD-10 diagnostic code I33) between 1998 and 2019. These data show stable incidence between 1998–99 (26.6 cases per million) and 2009–10 (26.9 cases per million), but an 86% increase to 50.0 cases per million in 2018–19 (figure).

One hypothesised cause of infective endocarditis is oral pathogens entering the bloodstream during invasive dental procedures. Consequently, use of

antibiotics before invasive dental procedures in patients who are at risk is a long-held preventive measure; however, antibiotic prophylaxis remains controversial. Since 2007, international guidelines have recommended that antibiotic prophylaxis should be restricted to patients at the highest risk of adverse outcomes—ie, those with a history of infective endocarditis, prosthetic or repaired heart valves, or complex congenital heart disease. These guidelines reflect a scarcity of evidence for antibiotic prophylaxis effectiveness, concerns for risk of adverse drug reactions, and the possibility that antibiotic prophylaxis contributes to an ever increasing global

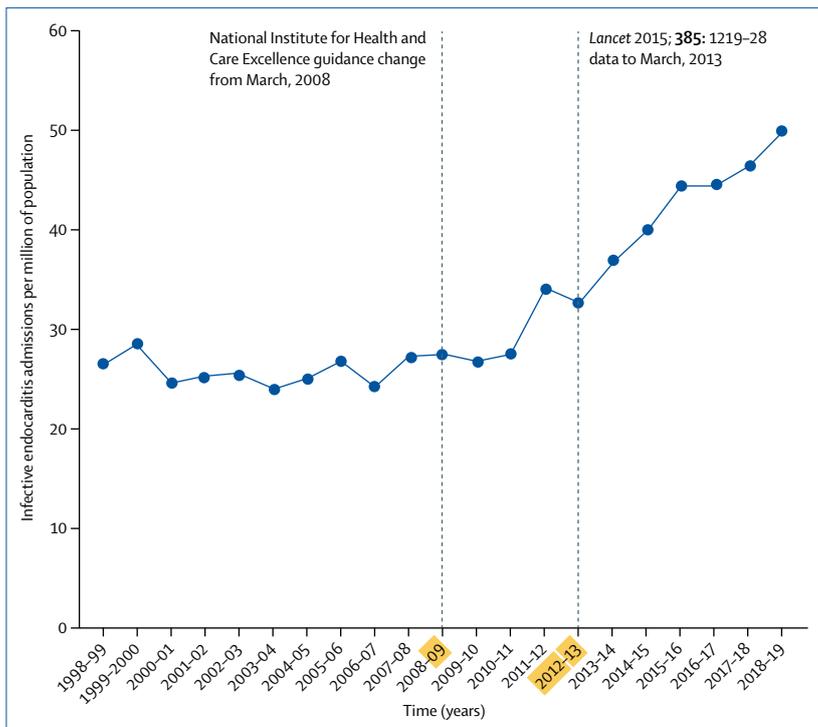


Figure: English hospital admissions with a primary diagnosis of infective endocarditis (ICD-10 diagnostic code I33) corrected for population growth

burden of antibiotic resistance. In March, 2008, however, the National Institute for Health and Care Excellence (NICE) boldly recommended complete cessation of antibiotic prophylaxis to prevent infective endocarditis in the UK, thereby creating conditions for a natural experiment of its effectiveness.

In 2015, our *Lancet* article<sup>3</sup> showed a large and significant ( $p < 0.0001$ ) decrease in antibiotic prophylaxis prescribing in England after implementation of NICE guidance and a parallel significant increase in incidence of infective endocarditis ( $p < 0.0001$ ) beyond the preceding upward trend. By March, 2013, there were 35 extra cases of infective endocarditis per month (419 cases per annum). Since then, NICE has acknowledged public and professional concern, and adjusted wording of their guidance to indicate that antibiotic prophylaxis is not routinely recommended.<sup>4,5</sup> Advice on the clinical implementation of this imprecise recommendation was subsequently provided by the Scottish Dental Clinical Effectiveness Programme<sup>6</sup> and endorsed by NICE and the British Cardiovascular Society; although, many dentists remain unaware of this advice.

In the absence of microbiological data, a rapidly increasing incidence of infective endocarditis cannot be attributed solely to cessation of antibiotic prophylaxis in the wake of the NICE recommendations. Multiple contributory factors are probable, including an ageing population, increased use of both intracardiac (eg, permanent pacemakers, implantable cardioverter defibrillators, or surgical and transcatheter heart valves) and vascular devices (eg, those used for chronic haemodialysis), epidemic levels of opioid addiction and associated injection drug use, emergence of staphylococci and enterococci (neither of which are targeted by antibiotic prophylaxis strategies) as more common causative organisms, and improved clinical awareness of infective endocarditis. Nevertheless, these findings are disturbing and contrast with reports of decreasing incidence in the USA<sup>7,10</sup> and decreasing or moderate increases in Europe,<sup>11-13</sup> where contributory factors are likely to be similar to those in England. Greater public health awareness and further investigation are warranted of the causes responsible for this alarming increase in the incidence of infective endocarditis in England, alongside renewed emphasis on education of patients at risk, maintenance of good oral hygiene, early disease diagnosis, timely referral, and specialist care.

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## European Green Deal: a major opportunity for health improvement



The European Green Deal<sup>1</sup> aims to respond to the escalating climate crisis by achieving net zero greenhouse gas (GHG) emissions from the EU by 2050. Current policies will achieve only 60% reductions by 2050 from 1990 levels, indicating the need for increased ambition. Additionally, the deal aspires to “protect the health and well-being of citizens from environment-related risks and impacts” and establish a toxic-free environment, deliver healthy and sustainable diets, and protect biodiversity.<sup>1</sup> This ambitious agenda would support planetary health.<sup>2</sup>

Europe alone cannot ensure that the global mean temperature increase is kept to below 2°C above pre-industrial levels as laid out in the Paris Climate Agreement,<sup>3</sup> but the EU's intention is to have a leadership role by cutting its own emissions rapidly and using its financial resources, knowledge, and influence to encourage other nations to increase their climate actions. The European Green Deal emphasises the importance of reducing the likelihood of GHG leakage—ie, more carbon-intensive imports to replace EU products from countries with lower ambitions for GHG-emission reduction—by ensuring that import prices reflect carbon footprints.

Many details of the proposals in the European Green Deal remain to be worked out, but, if successfully implemented, this deal has the potential to achieve major health improvements in the near term while reducing the growing health risks from climate change.<sup>4</sup>

The near-term health benefits can arise through successful policy implementation in sectors, such as the

energy, housing, transport, food, industry, and health-care sectors, that substantially contribute to emissions of carbon dioxide and short-lived climate pollutants like methane and black carbon.<sup>5</sup> Successful policies would reduce GHGs, fine particulate air pollution, and tropospheric ozone with major benefits to health. Replacing fossil fuels by clean renewable energy across these sectors could prevent about 3·6 million premature deaths annually worldwide (at 2015 population) from ischaemic heart disease (IHD), stroke, chronic obstructive pulmonary disease, and other causes, with about 430 000 of these premature deaths being in the EU.<sup>6</sup> When prevented deaths are valued using a standard economic approach (value of a statistical life),<sup>7</sup> economic benefits of reduced mortality substantially offset the costs of scaling up renewable energy.

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