

Trends in meningococcal disease: challenges in vaccine control when disease is rare

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In most wealthy and many middle-income countries, capsular group B *Neisseria meningitidis* (MenB) remains an important cause of invasive bacterial disease, particularly in the era of control of other major bacterial pathogens including MenC, *Haemophilus influenzae* type b and vaccine-type pneumococcus. The development of two new vaccines against MenB^{1,2} (with one or both now licensed in many countries) now provides the potential for a comprehensive approach to controlling these invasive bacterial pathogens. However, decisions to introduce vaccination at the population level are complex when there are low rates of disease, particularly when cost-effectiveness is considered³.

In this issue, xxxxx et al, discuss the epidemiology of meningococcal disease in Australia between 1999-2015, describing declining disease incidence, with historically low levels of infection in recent years, a pattern mirrored in other developed countries⁴. In addition to MenC vaccines, environmental interventions, including reductions in air pollution and the introduction of a smoking ban in public places⁵, have probably contributed to these declines seen in industrialised nations. However, these are not the only drivers. Data from long-established surveillance systems show patterns of peaks and troughs in rates of disease every few decades⁶. This is likely the result of an interaction between the (disease-associated) fitness of the prevalent clones and population immunity, which is acquired through nasopharyngeal colonisation and reduces the circulation of these clones over time⁷. Without vaccination or reductions in risk factors for transmission and disease, the arrival of a new strain, against which population immunity is limited, will likely lead to increased disease. In the UK, a recent rise in disease caused by a highly invasive capsular group W clone of *N. meningitidis* provides contemporary proof of the point^{8,9}. Australian public health officials should continue to watch the rise of W described in xxx et al's paper since this became the leading cause of meningococcal disease on the continent in 2016¹⁰, and be prepared to intervene, since this is the same clone that has shown a high attack rate in the UK and parts of Latin America,

necessitating new control programmes¹¹. It is noteworthy that this particular capsular group W strain might be controlled by use of the new MenB vaccine¹², which is the focus of this article.

Xxxx et al discuss the decision to not fund MenB vaccination through the National Immunisation Programme in Australia because of the current low incidence of disease; in the period 2005-2016 the attack rate for MenB disease in children <1 year of age was around 10/100,000. In comparison, rates in the UK were around 45/100,000 in 2006/7 in this age group falling to approximately 20/100,000 in 2015/16¹³. Such differences in disease epidemiology over time and between countries highlight the difficulty faced by policymakers when dealing with future uncertainty in planning vaccine programmes. A decision to fund would likely be more favourable if discussions happened at a time of high disease incidence.

Infants in Australia, as in the UK, have the highest rate of meningococcal disease, making this group the most obvious target for vaccination. Indeed, in the UK, MenB vaccination was introduced into the national immunisation programme in September 2015 for infants. The decision was not straightforward as there was considerable uncertainty about the protection that would be afforded by vaccination and about the costs, both in health and monetary terms, of the disease. Emerging post-implementation data indicate the vaccine has high effectiveness against invasive disease¹⁴, closely matching some of the more optimistic scenarios considered before introduction³. These data reduce some of the uncertainty about vaccine impact for countries still considering implementation and provide confirmation of the approach used in cost-effectiveness analyses in the UK that supported funding of the national programme, and indicated that the vaccine would be cost-effective at a low vaccine price. The duration of protection will become apparent with time following the UK introduction, but since the highest attack rate is in the first 2 years of life, a moderate duration of protection could provide substantial impact. Another issue which concerns policymakers is the association of the vaccine with febrile reactions around the time of immunisation¹⁵, which is mitigated to some extent by the use of prophylactic anti-pyretic medication as is recommended in the UK¹⁶.

Perhaps the most important observation from xxxx et al's study is the disparity between populations in Australia in both disease incidence and access to immunisation on the private market, which may lead to a serious inequity in access to public health between the rich and poor. Immunisation of this population was considered in Australia but not recommended in view of the uncertain efficacy and cost-effectiveness¹⁷, though at least the first of these points is now addressed by the emerging UK data¹⁴. Some of the highest contemporary disease rates in the developed world are documented in this article among Australian indigenous peoples with an incidence rate of 32.47/100,000 among infants <1 year of age, similar to rates observed among infants in the UK during this period¹³. High rates of disease in population sub-groups have been well described for meningococcal disease, including the exceptional disease rates affecting Maoris and Pacific Islanders in New Zealand¹⁸. Immunisation programmes targeting risk groups can be difficult to implement and sustain, but such disparity in health should not be ignored, when an effective intervention is available.

Declarations of interest statement

AJP has previously conducted studies on behalf of Oxford University funded by vaccine manufacturers, but currently does not undertake industry funded clinical trials. Trials of vaccines or observational studies previously funded by Okairos, Novartis, Pfizer were completed within the past 3 years. His department received unrestricted educational grants from Pfizer/GSK/Astra Zeneca in

July 2016 for a course on Infection and Immunity in Children. AJP chairs the UK Department of Health's (DH) Joint Committee on Vaccination and Immunisation (JCVI) and is a member of the World Health Organization's (WHO) Strategic Advisory Group of Experts.

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