Immunisation against meningococcus B

In their Comment (Aug 3, p 369)1 Richard Moxon and Matthew Snape ask “What now?” The key issue with meningococcal and other bacterial vaccines directed against organisms whose natural habitat is the upper respiratory tract is whether they affect transmission. This capability was key to the success of the meningococcus C (MenC) vaccines which were introduced in 2000 under circumstances of uncertainty about efficacy and low (but in that case rising) disease incidence. A decision to introduce the Novartis vaccine, which is not really a meningococcal B but actually a broader, generic meningococcal vaccine, and to give it to adolescents and young adults who have the highest carriage rates could have been followed by ecological studies to observe trends in total meningococcal carriage rates, as was done following the MenC catch-up in 2000.2 If the recent interim decision by the UK Joint Committee on Vaccination and Immunisation is confirmed, epidemiological studies following general vaccine introduction are presently off the table, but the question nevertheless urgently needs to be settled.

Answers could be rapidly obtained with a large cluster randomised carriage study in secondary schools alongside the MenC booster, which is about to be introduced. This study could be designed to measure both any direct and any indirect effects of the vaccine on carriage. It would certainly also make good sense to establish in advance whether the unequivocal demonstration of a biological effect on meningococcal carriage would drive a conclusion that vaccine use would meet NHS cost-benefit thresholds at a price greater than zero.

We believe this issue is of great importance not only for the fate of this particular meningococcal vaccine, but also for that of vaccines that may affect carriage and transmission of other pathogens that are currently under development.

The University of Bristol and University Hospitals Bristol NHS Trust have received funding from Novartis and manufacturers of other meningococcal vaccines for clinical research, consultancy, and speaking engagements undertaken by RM. RM is a member of the Merck US pediatric vaccines advisory board. He has provided consultancy to Merck and GlaxoSmithKline on vaccine-related topics. He is on the scientific advisory boards of Genocia Biosciences and Anasis Biosciences, and is a named co-inventor on several vaccine-related patents.

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As the UK’s largest and longest established meningitis charity, Meningitis Trust/Meningitis UK is disappointed with the UK Joint Committee on Vaccination and Immunisation (JCVI) decision not to recommend the 4CMenB vaccine for use in the routine immunisation programme.

We acknowledge the importance of more data on efficacy, duration of protection, and impact on carriage, and wholeheartedly support the need for a population-based evaluation. We are calling for the urgent introduction of this life-saving meningococcal B vaccine for babies and adolescents on a population evaluation basis. We feel strongly that this would meet the JCVI need to collect further data, while simultaneously saving lives.

We ask that the Department of Health, Public Health England, NHS England, and Novartis—as the manufacturer of 4CMenB, licensed as Bexsero—work together to agree how adoption of the vaccine can be achieved quickly; any loss of time means loss of lives.

The government has set great store by improving the NHS ability to adopt innovative medicines through initiatives such as Commissioning Through Evaluation. The JCVI themselves have highlighted that the infrastructure and expertise available in the UK would make this country the ideal setting for a population-based evaluation. In November, 1999, a decision was made to introduce the meningococcal C vaccine in the routine schedule and implement a catch-up campaign for everyone aged 18 years and younger. At the time, there was a lack of published evidence on efficacy and effect on
Carriage. Nonetheless, the vaccine was introduced and proved to be a major public health success, preventing many deaths and lifelong disability.

It is crucial that no more time is wasted in obtaining the data needed, both for those who will continue to be affected by this devastating disease until the vaccine is in routine use, and also for the future of vaccine research and development. As a stakeholder, we will formally respond to the JCVI draft recommendation by September 3, 2013.

I declare that I have no conflicts of interest.

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The decision by the UK Joint Committee on Vaccination and Immunisation (JCVI) not to recommend routine vaccination with a new vaccine against meningococcus B is a reflection of the growing weight of economic issues in decisions about vaccine use. The relative low frequency of meningococcal disease in infancy similarly played a major part in the decision by the US Advisory Committee for Immunization Practices (ACIP) not to recommend routine vaccination of infants against meningococcal groups A, C, W-135, and Y infection. Although the cost of public health programmes cannot be ignored in these troubled economic times, the high mortality and serious sequelae of meningococcal infections should also be taken into account despite their low incidence. Even if the JCVI and the ACIP do not believe that their respective governments can afford the costs, parents should be informed about the availability of the vaccines and the reasons why the committees declined to recommend them universally.

I suspect that re-evaluation will be necessary once the duration of protection and the effect on pharyngeal carriage induced by the meningococcal vaccines have been established, and indeed the JCVI report does suggest that recommendations will be reconsidered once additional studies have been done with the new meningococcal B vaccine.

There is another aspect that should concern us. Considering that the development of a new vaccine costs at least half a billion US dollars, vaccine manufacturers must make choices. Bodies like the JCVI and ACIP should give prospective advice to manufacturers about which vaccines are of interest and will be recommended. This is not a question of protecting profits by manufacturers, but rather the reality that only a limited number of vaccines can be developed, and it is in the interests of all of us that development leads to widespread use and control of disease.

I have received honoraria and consultancies from major vaccines manufacturers, including Novartis, Sanofi, and GSK.

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Meningococcus is a cause of severe life-threatening infections, which, despite advances in medical technology, result in a mortality rate of up to 10% and leave up to 50% of individuals with lifelong disabilities. Several meningococcal groups, including meningococcus C (virtually eradicated in the UK after introduction of a vaccine) and meningococcus B, can cause meningococcal disease. Until recently, meningococcus B has eluded our ability to develop a vaccine. However, such a vaccine (4CMenB) has recently been licensed by the European Medicine Agency. The UK Joint Committee on Vaccination and Immunisation (JCVI) concluded that this vaccine is not cost effective based on their own internal analysis. Although, as Richard Moxon and Matthew Snape point out in their Comment, statements from the same academic institutions that developed the internal JCVI report contradict this conclusion. This can be explained by the nature of cost-effectiveness analyses done before introduction of the vaccine. For pneumococcal conjugate vaccine in the USA, the cost per quality-adjusted life-year (QALY) saved was estimated to be more than US$80 000 in the prelicensure analysis, but this fell ten-fold when the true effect of the vaccine was known after introduction. An example in the opposite direction was the cost-effectiveness analysis of varicella vaccine, which was based on a one-dose schedule—we now know that two doses of vaccine are required, which doubles the cost.

Although it is tempting to consider cost-effectiveness analyses as an easy decision tool for vaccines, for several recently licensed vaccines the results of such analyses have been wrong and misleading. We should return to viewing the potential to prevent needless suffering and death as the primary goal of vaccination and make decisions on this basis. In view of their poor reliability, cost-effectiveness analyses done before introduction of vaccines should be interpreted with caution and should not be used as primary decision-making criteria.

I am a consultant for Novartis Vaccines and serve on the Independent Data Monitoring Committee for WHO and GSK.

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Department of Error

Cotter C, Sturrock H, Hsiang MS, et al. The changing epidemiology of malaria elimination: new strategies for new challenges. Lancet 2013; 382: 909–12—Two affiliations were missing from this Review. The affiliations details should have read “The Global Health Group (C Cotter MPH, H J Sturrock PhD, M S Hsiang MD, J Liu PhD, A A Phillips BA, J Hvango MD, C Smith Gueye MPH, N Fullman MPH, R D Gosling MD, Prof Sir R G A Feachem DSc[Med] and Department of Pediatrics (M S Hsiang), University of California, San Francisco, CA, USA; and Malaria Branch, Centers for Disease Control and Prevention, Atlanta, GA, USA (J Hvango)”. These corrections have been made to the online version as of April 26, 2013, and have been made to the printed Review.