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EDITORIALS

Introducing a new group B meningococcus vaccine

Many forces affect the final decision

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The introduction of a new vaccine is highly complex, particularly a new category of vaccine with no biological precedent. The new group B meningococcus vaccine Bexsero (4CMenB),[1] developed using a genomic based reverse vaccinology approach,[2] is a case in point. When a vaccine is targeted against a relatively common disease, the company usually sponsors a large randomised controlled trial to show that the vaccine works. Group B meningococcal infection is sufficiently rare, however, that such a trial is not feasible.

In most countries, advice on vaccines and immunisation programmes is given to governments by independent committees. This advice includes data on vaccine effectiveness, the likelihood that the vaccine will confer herd immunity (protect some unimmunised people by reducing carriage or spread of disease), safety, and cost effectiveness. In the United Kingdom, the Joint Committee on Vaccination and Immunisation (JCVI) has such a role. In the UK,[3] and in Australia, Canada, the United States, and many European countries, the government is not permitted in law to fund an immunisation programme unless the immunisation advisory committee says it is cost effective.

Different countries allow different assumptions in the modelling, so they do not always reach the same decision. The process usefully distances the government from the decision, which is made on scientific and economic grounds. Decisions are made on quality adjusted life years (QALYs), but this does not account for the politics.[4] Health economists ask what health benefit we get from buying a vaccine. Politicians may want to buy votes as well and are fearful of losing them if they do not bow to pressure. Pressure comes from patient groups and doctors, who understandably advocate for their patients. Drug companies know the power of such advocacy and are increasingly adept at stoking the fire using advertising agencies and media campaigns. This may distort the decision making process in such a complex area.

4CMenB was considered by the JCVI, which used data on immunogenicity and possible herd immunity to model the likely extent of protection. In July 2013, the committee published an interim statement advising that 4CMenB "would not be cost effective in an infant immunisation schedule at any price."[5] This was a surprisingly strong statement: the committee said that, even if the vaccine were free, the cost of programme implementation and adverse events would outweigh any protection.

After an outcry,[6] the committee considered new data—including new modelling data and litigation costs for cases of meningococcal infection—and revised its decision.[1 7] In March 2014, the committee recommended a three dose infant programme if a cost effective price could be agreed"[7] The UK government immediately announced that the infant group B meningococcal vaccination programme would go ahead if a cost effective price could be agreed.

Predictably, the press announced the decision as if it were definite.[8] This must surely put extra pressure on the Department of Health when it negotiates the vaccine price with Novartis. Although transparency is laudable, the department might have reduced this pressure by delaying the announcement until a cost effective vaccine price had, or had not, been reached.

The introduction of 4CMenB vaccine in the UK would be beneficial and would inform the rest of the world about the true value of this new vaccine. The UK was the first country to pay for a group C meningococcal vaccine, a decision that was vindicated by finding that the vaccine was not only effective, but prevented infections in unimmunised people, and without serogroup replacement.[9] Children and adults in many other countries benefited from the data. However, the group C meningococcal vaccine is a conjugate vaccine, so there was prior proof of principle of action based on experience with the *Haemophilus influenzae* type b and pneumococcal vaccines. On the basis of projections of group B meningococcus coverage alone, it is highly unlikely that the 4CMenB vaccine will be nearly as effective. Even if vaccine efficacy is low, however, withdrawal of an established group B meningococcal vaccination programme would be difficult.

Does it really matter if the UK government pays too much for 4CMenB? There are some potential serious harms. Firstly, if

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governments bow to societal and corporate pressure, the benefit of maintaining the separation between science and state is undermined. The situation with expensive vaccines also applies to orphan drugs,[10] particularly those for cancer. The UK has already established a special cancer fund that spends £200m (€240m; $331m) annually to buy cost ineffective anti-cancer drugs.[11] Although the UK press has suggested conspiracy, the government and the JCVI strongly deny any government interference with the advisory process regarding 4CMenB.

Secondly, vaccines are given to a large number of people, so even if a small proportion experience adverse effects, the absolute number affected may be large. We live in an era of vaccine hesitancy and are intolerant of risk. The decision to move from whole cell pertussis vaccines to acellular ones, made on the basis of the reactogenicity of whole cell vaccines and limited data about duration of protection, is being called into question given concerns of reduced vaccine effectiveness.[12] Pertussis refuses to go away and infants still die from it despite high coverage.[12]

New vaccines need to be safe if we are to sustain public trust.[13] 4CMenB is a reactogenic vaccine with high rates of fever, and an increase in febrile convulsions is possible. If the vaccine causes measurable harms but its efficacy is low or uncertain, the public pressure for the vaccine may turn all too quickly to condemnation for putting so many children at risk. Immunisation programmes are sustainable only as long as the public trusts the vaccine involved.

Competing interests: We have read and understood the BMJ Group policy on declaration of interests and declare the following interests: DI and JMcV are both members of the Australian Technical Advisory Group on Immunisation. DI also sits on the Australian government's Pharmaceutical Benefits Advisory Committee. JMcV has undertaken a range of research on meningococcal infection and vaccines for Novartis (which produces Bexsero meningococcus vaccine) and for Wyeth (now Pfizer) vaccines, which has an alternative meningococcus group B vaccine in the pipeline.

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