Letters

Influenza vaccination: policy versus evidence

No gap between policy and evidence

SATURN STILLS/SPL

EDITOR—Jefferson believes that his systematic reviews show that influenza vaccines "have little or no effect on the effects measured."[1] He wonders why there is a gap between evidence and policy.

Jefferson identifies three reasons why his evidence contradicts policy.

Firstly, policy relies heavily on non-randomised studies. Yet his preference for randomised controlled trials is based on historical, pragmatic, and heuristic reasons and cannot be justified on epistemological grounds alone.[2] He argues that heterogeneity among studies and study years[3] can be overcome by "averaging" outcomes over several years, and finds observational studies yield relative risk reductions that are statistically significant.

Secondly, he cites the lack of evidence of vaccination on effects "at the centre of campaign objectives," yet he documents such evidence for older adults, barely fails to show it for younger adults, and is unable to consider influenza-related otitis media, a frequent complication in young children.

Thirdly, he is concerned that published studies lack safety data, but 300 million doses are used each year[4] and safety problems would not require a systematic review to be detected.

The goal of vaccination policy is not to "prevent seasonal outbreaks" of influenza[1] but to prevent costly influenza-related hospital admissions and deaths. In formulating policy, health officials consider three types of evidence.

Firstly, influenza vaccine must work, and randomised controlled trials provide this evidence.

Secondly, health officials must understand the population burden of disease and know whether it can be reduced by vaccination. Observational studies can help document reductions in attributable (not relative) risk following vaccination.[3 5]

Thirdly, health officials must know whether vaccination will be economically worth while, and evidence for this must come from other sources.[5]

There is no "gap between policy and evidence."[1] Systematic reviews can never provide the three types of evidence needed to formulate policy for influenza vaccination.

David S Fedson *retired physician*
01630 Sergy Haut, France
dfedson@wanadoo.fr

Kristin L Nichol *professor of medicine*
University of Minnesota

Competing interests: DSF has received honorariums from Sanofi Pasteur for lectures on influenza vaccination, and in 2003-4 served as a part time consultant to the Influenza Vaccine Supply International Task Force.

1 Jefferson T. Influenza vaccination: policy versus evidence. *BMJ* 2006;333:912-5. (28 October.)
2 Abel U, Koch A. The role of randomization in clinical studies: myths and beliefs. *J Clin Epidemiol* 1999;52:487-97.
3 Nichol KL. Heterogeneity of influenza case definitions and implications for interpreting and comparing study results. *Vaccine* 2006 [Epub ahead of print] doi:10.1016/j.vaccine.2006.05.064.
4 Macroepidemiology of Influenza Vaccination (MIV) Study Group. The macroepidemiology of influenza vaccination in 56 countries, 1997-2003. *Vaccine* 2005; 23:5133-43.
5 Nichol KL. The efficacy, effectiveness and cost-effectiveness of inactivated influenza virus vaccines. *Vaccine* 2003;21:1769-75.

Protection from disease versus disease severity

EDITOR—Jefferson writes that it is impossible for a vaccine that does not prevent influenza to prevent its complications, including admission to hospital.[1] This is clearly wrong.

It is well known that immunity induced by some vaccines (and also by some natural infections) does not necessarily protect against (re-)infection. Immunologists distinguish between so called sterilising immunity, which completely prevents replication of an intruding virus, and "non-sterilising" immunity, in which replication of the pathogen can still occur, but its spread and thus induction of disease symptoms may be reduced. To prevent severe forms of disease and the likelihood of complications such as secondary infections can be a meaningful objective for a vaccine, even though the vaccine may not be able to protect against infection and milder forms of the disease. The author's misjudgment as expressed by the cited statement makes me wonder about the plausibility of his interpretation of the existing data.

Christian W Mandl *professor of virology*
Medical University of Vienna, A-1095 Vienna, Austria
christian.mandl@meduniwien.ac.at

Competing interests: None declared.

1 Jefferson T. Influenza vaccination: policy versus evidence. *BMJ* 2006; 333:912-5. (28 October.)

Policy is in the lead

EDITOR—In his review of the available literature, Jefferson finds a large gap between influenza vaccination policy and what the data tell us.[1] What the data tell us, he writes, is that the inactivated vaccines have little or no effect on the effects measured, and the comparative evidence is insufficient to demonstrate the vaccines are safe.

Jefferson's results are consistent with previous epidemiological reviews of the effects of influenza vaccination. A 2005 US National Institutes of Health review of over 30 influenza seasons could not correlate increasing vaccination coverage after 1980 with declining mortality rates in any age group and concluded that observational studies substantially overestimate vaccination benefit.[2]

Annually, public health agencies in the United States and United Kingdom launch massive campaigns aimed at convincing doctors of the importance of influenza vaccination. Is this necessary? Safe and effective interventions for diseases that truly pose a threat to morbidity and mortality are unlikely to be controversial. Not only is the evidence supporting the safety and effectiveness of influenza vaccination lacking, but there are also reasons to doubt conventional estimates of the mortality burden of influenza. As I have documented previously,[3] the mortality data are a mess—over the period in which the Centers for Disease Control and Prevention's statistical modelling of flu-associated mortality has estimated an 80% rise in deaths, officially recorded flu deaths have dropped by 30%. Complicating this is the fact that influenza-like illness is not only indistinguishable from influenza, but far more common, leading to unrealistic expectations of influenza vaccination.

The policy questions raised by these reviews are crucial to answer. While it is

bmj.com

We select the letters for these pages from the rapid responses posted on bmj.com, favouring those received within five days of publication of the article to which they refer.

Letters are thus an early selection of rapid responses on a particular topic. Readers should consult the website for the full list of responses and any authors' replies, which usually arrive after our selection.

often said that influenza poses a serious burden to health, influenza vaccines impose their own particular burden—to the tune of billions of dollars annually. If policy is going to be driven by evidence, this requires us, first of all, to consider the evidence.

Peter Doshi *graduate student*
Massachusetts Institute of Technology, Cambridge, MA, USA
pnd@mit.edu

Competing interests: None declared.

1 Jefferson T. Influenza vaccination: policy versus evidence. *BMJ* 2006;333:912-5. (28 October.)
2 Simonsen L, Reichert TA, Viboud C, Blackwelder WC, Taylor RJ, Miller MA. Impact of influenza vaccination on seasonal mortality in the US elderly population. *Arch Intern Med* 2005;165:265-72.
3 Doshi P. Are US flu death figures more PR than science? *BMJ* 2005;331:1412.

Vested interests will always trump evidence

Editor—With reference to the article by Jefferson,[1] five years ago I asked my general practitioner what the facts were about the pros and cons of flu vaccination, and I was referred to the handouts from the Department of Health. These were long on assertion and short on facts. I embarked on a literature search and running correspondence with various civil service mandarins with the limited ambition of getting data on what actual tests—of efficacy and safety—had been done on current vaccines and with what results. After much evasive action and stalling I was informed that such information was confidential.

The *Lancet* published my scepticism about the extraordinary claims being made for the ability of flu vaccine to prevent not only the flu but death as well, whatever the cause.[2] Since then a few papers have expressed concern about the inconclusive nature of the evidence for its efficacy,[3 4] and the public has been exhorted repeatedly to "protect themselves."

The enormous expense of this futile exercise doesn't seem to register—partly, I fear, because of payment inducements offered to general practitioners. They, perhaps, may claim they believed the recommendations of the Department of Health and carried out the vaccination programmes in good faith. This excuse—"only carrying out orders"—is of doubtful validity. There can be no excuse for the harmful public health decisions and refusal to come clean about what precisely were the reasons for them. It is too much to hope for repentance and reversal, however. The Faustian contract exemplified in the structure of the Medicines and Healthcare products Regulatory Agency will see to that.

G H Hall *retired physician*
Exeter EX1 2HW
h.2@which.net

Competing interests: None declared.

1 Jefferson T. Influenza vaccination: policy versus evidence. *BMJ* 2006;333:912-5. (28 October.)
2 Hall GH. Antiflu, or antideath vaccination? *Lancet* 2001:357:2141.
3 Van der Wouden JC, Bueving HJ, Poole P. Preventing influenza: an overview of systematic reviews. *Respir Med* 2005;99:1341-9.
4 Simonsen L, Reichert TA, Viboud C, Blackwelder WC, Taylor RJ, Miller MA. Impact of influenza vaccination on seasonal mortality in the US elderly population. *Arch Intern Med* 2005;165:265-72.

Word limits best explain failings of industry supported meta-analyses

Editor—Although few doubt that industry funded systematic reviews sometimes use poor methods and misrepresent findings, Jørgensen et al overestimate this bias and misattribute differences in methods and reporting to it.[1] Median quality scores of the included reviews were 7 for Cochrane reviews, and 2, 2, and 3 for industry funded, undeclared funding and non-profit or no funding journal reviews. These results are best explained by word restrictions, not financial support. For example, the *BMJ* paper and online versions of the included celecoxib review were restricted to 2211 and 3425 words,[2] whereas the unrestricted Cochrane review has 6002 words.[3]

The reliability of unblinded quality assessments raises concern, at least for the celecoxib reviews. Contrary to the findings of Jørgensen et al, the reviews gave equivalent detail concerning allocation concealment, and the industry funded review contained four paragraphs with reservations about results. Interestingly, the *BMJ* deleted two of these paragraphs to shorten the review for the paper journal. Had Jørgensen's study only included published reviews, the comparison by funding source could have been blinded and controlled for word length.

The industry celecoxib review was produced by an experienced Cochrane reviewer, protected from industry interference by a contract allowing freedom to publish (including results of previously unpublished trials). Data were extracted from full industry reports, avoiding problems extracting detail from abridged journal articles, such as the *JAMA* report of the CLASS trial.[4] The Cochrane review did not have access to this level of information.

Assessment of the likelihood of bias in reviews, including Cochrane reviews, should always be based on the methods and completeness of results, not on prejudices about the organisations from which they emanate. The lesson from the paper by Jørgensen et al may be more that journals should reverse the trend of reducing word lengths, and give authors the opportunity to explain methods in the detail afforded by the Cochrane review format.

Jonathan J Deeks *professor of health statistics*
Department of Public Health and Epidemiology, University of Birmingham, Birmingham B15 2TT
j.deeks@bham.ac.uk

Competing interests: JJD has contributed to the Cochrane Collaboration for over a decade, is currently a member of the steering group of the Cochrane Collaboration and Treasurer. He has co-authored 14 Cochrane reviews, and is the lead editor of the statistical section of the *Cochrane Handbook*. The views expressed here are his own and not necessarily those of the Cochrane Collaboration. His previous unit (Centre for Statistics in Medicine, Oxford) received funding from Pfizer and Searle to undertake the review mentioned in reference 2 and JJD received consultancy fees from Pfizer from 2001-2. Both his previous and current units have received royalties from the *BMJ* on sales of reprints of reference 2.

1 Jørgensen AW, Hilden J, Gøtzsche PC. Cochrane reviews compared with industry supported meta-analyses and other meta-analyses of the same drugs: systematic reviews. *BMJ* 2006:333:782-5. (14 October.)
2 Deeks JJ, Smith LA, Bradley MD. Efficacy, tolerability, and upper gastrointestinal safety of celecoxib for treatment of osteoarthritis and rheumatoid arthritis: systematic review of randomised controlled trials. *BMJ* 2002;325:619.
3 Garner SE, Fidan DD, Frankish RR, Judd MG, Shea BJ, Towheed TE, et al. Celecoxib for rheumatoid arthritis. *Cochrane Database Syst Rev* 2002;4:CD003831.
4 Silverstein FE, Faich G, Goldstein JL, Simon LS, Pincus T, Whelton A, et al. Gastrointestinal toxicity with celecoxib vs nonsteroidal anti-inflammatory drugs for osteoarthritis and rheumatoid arthritis: the CLASS study: a randomized controlled trial. celecoxib long-term arthritis safety study. *JAMA* 2000;284:1247-55.

Measles outbreak in Surrey

Editor—Asaria and MacMahon discuss measles in the United Kingdom.[1] An outbreak of measles in South Yorkshire this year had 97 suspected and at least 37 confirmed cases reported.[2]

In Surrey, the first confirmed case occurred in a child in January 2006. The number of measles cases notified to the Surrey and Sussex Health Protection Unit increased during the week of 13 March 2006, and an initial outbreak meeting was convened on 16 March.

By the end of August 2006, the unit had received 280 notifications of measles in Surrey residents, with 111 confirmed or epidemiologically linked cases. This compares with a total of six cases in the county during 2005.

Twenty four patients were admitted, and four cases were confirmed in healthcare workers. Sixteen doses of human normal immunoglobulin were required as post-exposure prophylaxis for vulnerable contacts.

Sensitive contact tracing was carried out, and measures implemented to reduce further spread. The unit also sent out letters to all schools in Surrey, to the primary care trust, and liaised with occupational health for the acute and primary care trusts. We used media attention to raise awareness of the need for vaccination. The unit has developed an algorithm for the management of measles in primary care, which we used.[3 4]

One of our cases was a young mother with a baby aged under 6 months. Despite having been given human normal immunoglobulin, the baby subsequently developed measles. It has hitherto been assumed that most mothers would be immune to measles through natural illness or vaccination, and that babies under the age of 6 months would be protected by maternal antibodies. This can no longer be assumed, as measles has been uncommon in the UK for so many years. Babies

under 6 months should be offered HNIG if the mother is thought unlikely to be immune.

Peter M English *consultant in communicable disease control*
peter.english@shpu.nhs.uk

Nicola Lang
Anna Raleigh
Kevin Carroll
Margot Nicholls
Surrey and Sussex Health Protection Unit, Cedar Court, Leatherhead KT22 9RX

Competing interests: None declared.

1 Asaria P, MacMahon E. Measles in the United Kingdom: can we eradicate it by 2010? *BMJ* 2006;333:890-5. (28 October.)
2 Health Protection Agency. Outbreak of measles in Doncaster. *Commun Dis Rep Wkly* 2006;16:3-4. www.hpa.org.uk/cdr/archives/2006/cdr1506.pdf (accessed 2 November.)
3 Carroll K, English PMB, Morgan J, Nicholls M, van den Bosch C. *Control of measles in the event of an outbreak*. Leatherhead: Surrey and Sussex Health Protection Unit, 2006:1-10. www.bigfoot.com/~scdcs (follow "Policy and guidance documents"; accessed 2 Nov 2006).
4 Department of Health, Welsh Office, Scottish Office Department of Health, DHSS (Northern Ireland). Immunisation against infectious disease: the "Green Book" draft chapter on measles (available from website). In: Department of Health, Welsh Office, Scottish Office Department of Health, Ireland) DN, eds. *Immunisation Against Infectious Disease—"The Green Book."* London: Department of Health, 2006. www.publications.doh.gov.uk/greenbook. Updated August 2006 (accessed 31 Oct 2006).

Community acceptance is needed to eradicate polio in India

Editor—Zaracostas identifies the importance of ensuring a successful campaign against polio eradication and the possible catastrophes of a failed one.[1] We disagree on the four key factors for polio eradication, in that both community acceptance and political will are major issues in India.

In India, the highest numbers of cases occur in the districts of western Uttar Pradesh followed by Bihar.[2] A similar problem to the one encountered in Nigeria in late 2003 is also being seen in these parts of India. Misleading and untrue information of a potential association between oral polio drops and sterility is being spread among many Muslim communities by various community leaders and several related and unrelated agencies. This is leading to a widespread non-acceptance of the programme in this particular community and consequently has resulted in the increase in the number of cases of polio, notably in western Uttar Pradesh. This year too most cases are from the same region.[2] The stakeholders are doing their best to manage the situation and the shift to the use of monovalent oral polio vaccine from the conventional trivalent oral polio vaccine is a reflection of this.

However, without engaging the communities and without a great deal of political will very little success will be seen in these provinces.

Anandagiri M Shankar *specialist registrar in public health medicine*
giri.shankar@walsall.nhs.uk

Sam Ramaiah *director of public health medicine*
Walsall Teaching Primary Care Trust, Walsall WS1 1TE

Competing interests: None declared.

1 Zaracostas J. Failed vaccine campaigns may lead to polio resurgence, experts warn. *BMJ* 2006; 333: 823. (21 October.)
2 AFP Surveillance Bulletin—India. GoI/NPSP: report for week 40, ending 7 October 2006. www.npspindia.org/bulletin.pdf (accessed 23 Oct 2006).

Reconstructive surgery is often needed after obesity surgery

Editor—Kral discusses the surgical management of obesity and the many benefits but did not mention post-bariatric reconstructive surgery.[1] After bariatric surgery, patients usually experience a drastic loss of weight (50-70 kg is a common amount in our experience) over a very short period of time, for which the elasticity in their skin cannot compensate. This leaves them with festoons of redundant skin and subcutaneous tissue, which has a major effect on the quality of their lives and their function.

These skin folds appear characteristically in the abdomen, the upper arms and thighs, and the lateral chest and hips, and they cause a constellation of problems for patients, ranging from chronic skinfold intertrigo and infections, inability to find clothing that fits, to causing a mechanical impediment to exercise or to performing physical labour and earning a living. Many patients report an aversion to being seen naked or to indulging in sexual relationships with partners—problems they did not have when they were morbidly obese before their surgery. These problems blight the benefits that patients derive from bariatric surgery and may inhibit continuing loss down to goal weight.

Plastic and reconstructive surgery after weight loss to return patients to a normal function and aesthetic form is as pivotal to bariatric surgery as reconstruction after mastectomy is in the surgical management of breast cancer. Various approaches exist for post-bariatric reconstruction, which will depend on local expertise and facilities and the preferences and priorities of the patient and the surgeon. Typically patients may need surgery to the abdomen, lower back, buttocks, upper arms, thighs, and breasts, which will usually be staged and combined over several operations.

Chidi C Ekwobi *registrar*
chidi.e@ukonline.co.uk

Adam R Greenbaum *consultant*
Department of Plastic Surgery, St Thomas' Hospital, London SE1 7EH

Competing interests: None declared.

1 Kral JG. ABC of obesity: Management: Part III—Surgery. *BMJ* 2006;333:900-3. (28 October.)

Humanitarian aid starts at home

Editor—Humanitarian aid has become more politicised.[1] Humanitarian workers can reverse this trend only if governments or decision makers are held accountable for their decisions.

ASSIST is a primary care service delivering primary care services solely for asylum seekers. It has seen a huge upsurge in the numbers of failed asylum seekers in the past year (which also is reflected nationally). For complex and varied reasons, most of these patients are or will become destitute. They still need health care at all levels despite not being entitled to anything except in extremis because of their failed status. This client group is the most vulnerable in our society and yet often the most neglected and ignored.

The provision of humanitarian aid to those who are most needy and how we respond to those who are most vulnerable are at the core of how we judge our own society. World disasters seem to dominate our media and invoke a response. Why can't we invoke such a response on our own doorstop to those who are equally deserving?

Les Ashton *general practitioner*
ASSIST, Primary care service for asylum seekers, Leicester LE1 2NZ
lesashton@ntlworld.com

Competing interests: None declared.

1 Brennan RJ, Sondorp E. Humanitarian aid: some political realities. *BMJ* 2006;333:817-8. (21 October.)

The full English: the full picture

Editor—Spence is right about tackling obesity, but, to continue the metaphor, it's not just public health that needs to stop fiddling while Rome burns.[1] A lot of fruitless effort has been spent to promote the "right" behaviours at an individual level, and to endorse the importance of "making the healthy choice the easy choice."

Meanwhile, back in the real world, many people struggle to make sense of an increasingly inequitable, consumerist society driven by an insatiable appetite for economic growth. Arguably, obesity and climate change are just two of many adverse consequences of the trajectory we are currently following.

Let's cycle to work or take a healthy holiday if we can, but let's also ignite the debate about these issues. We are part of a group of public health specialists who are challenging the current healthy choice agenda (www.healthyfuture.org.uk).[2] Spence and others are welcome to join us physically or virtually.

Fiona Crawford *public health programme manager*
fiona.colin.kirsty@ntlworld.com

Pauline Craig
Glasgow Centre for Population Health, Glasgow

Competing interests: None declared.

1 Spence D. The full English. *BMJ* 2006;333:925. (28 October.)
2 Ogilvie D, Hamlet N. Obesity: the elephant in the corner. *BMJ* 2005;331:1545-8.