**COMPARING HPV VACCINES**

**HPV vaccine prices in Italy**

In contrast to what was reported in the editorial, both the bivalent (Cervarix) and the quadrivalent (Gardasil) vaccines are used in Italy for the campaign against cervical cancer. Most of the 20 Italian regions, which fund and implement vaccination programmes on their territory, ran single tenders to exploit potential competition between the two vaccine manufacturers. A few regional tenders took account of genital wart protection too, assigning slightly higher marks in the bid for the quadrivalent vaccine because of this.

Although tender prices varied widely, the average had dropped to around €55 (£48; $76) per dose by the end of 2009, much lower than the original ex-factory prices negotiated by Aifa (Italian agency for drugs) for Cervarix (€95) and Gardasil (€104). A closer look at the regional price patterns for the two vaccines separately indicated that the quadrivalent vaccine was the cheapest after two years of tendering.

The Italian experience shows that tendering can achieve worthwhile price reductions even when competition is minimal—only two manufacturers produced their own vaccines that were judged equivalent for the major health goal (cervical cancer in this case).

Thus, the key determinant of cost effectiveness is hard to assess, making published economic evaluations mainly exercises in long term forecasting, and not very useful for public policy purposes. Health authorities can achieve an acceptable cost effectiveness ratio only by striving for sustainable prices and assuring high coverage rates.

Livio Garattini director lgarattini@marionegriti.it
Katie van de Vooren researcher

**UK needs vaccine to protect against HPV types causing RRP**

We are pleased that the Department of Health is reviewing which human papillomavirus (HPV) vaccine to use in the national immunisation programme. As Jit and colleagues state, deciding between the bivalent and the quadrivalent vaccine is not straightforward. We would like to contribute to the decision making process by highlighting our experience of treating patients with recurrent respiratory papillomatosis (RRP), a disease in which warts grow within the airway epithelium.

The quadrivalent vaccine is 99% effective at preventing genital warts caused by HPV types 6 and 11. Because RRP in children probably results from transmission of these HPV types from the mother, we agree that the incidence of RRP will probably decrease at the same rate as genital warts after the quadrivalent vaccine is introduced. The burden of RRP on patients and their families is clear. A survey of UK otolaryngologists identified 600 people treated for RRP over 10 years; 9% of children in this survey needed a tracheostomy and 2% died of their disease. Surgery is the only effective treatment, but the warts typically recur; on average, children need two operations under general anaesthesia each year, with some needing hundreds of operations over their lifetime.

We are concerned that if the UK does not adopt a vaccine that protects against HPV types 6 and 11, we may continue to see patients with RRP when the disease has disappeared in other countries.

Michael P Rothera president mprothera@aol.com
David M Albert immediate past president, British Association for Paediatric Otorhinolaryngology (BAPO), UK
Owain H Hughes clinical research fellow, University College London Institute of Child Health and Great Ormond Street Hospital, London, UK

**Chasing face of HPV related cancer in the UK**

As the UK nears a decision on continuation of the national human papillomavirus (HPV) vaccination programme, Jit and colleagues’ economic evaluation of the available vaccines makes compelling reading. When developing arguments for cost effectiveness of the bivalent and quadrivalent vaccines, the analysis bears heavily on available data for cervical cancer, and to a lesser extent other HPV related anogenital malignancies. Recent publications on the influence of HPV type 16 on oropharyngeal squamous cell carcinoma (OPSCC) in the UK came too late to be considered in the analysis, but both publications show that most OPSCCs are now HPV positive.

Should this trend continue, then the latest American predictions that HPV positive OPSCC cases will exceed those of cervical cancer by 2020 may come true in the UK. Jit and colleagues acknowledge a previous lack of consensus among epidemiologists on the influence of HPV at other tumour sites. However, in our opinion, the statement that “possible protection against non-cervical cancers, while a

1 Verheijen R. Comparing bivalent and quadrivalent HPV vaccines Modelling can help, but the tender price determines cost. BMJ 2011; 343:d5720. (27 September.)
2 Garattini L, van de Vooren K, Curto A. Pricing HPV vaccines, lessons from Italy. Pharmacoeconomics (forthcoming).

2 FUTURE (H1 Study Group. Four-year efficacy of prophylactic human papillomavirus quadrivalent vaccine against low grade cervical, vulvar, and vaginal intraepithelial neoplasia and anogenital warts: randomised controlled trial. BMJ 2010;341:c3483.

Cite this as: BMJ 2011;343:d6668

**LETTERS**

Cite this as: BMJ 2011;343:d6672
substantial benefit, is less important in economic (cost and quality of life) terms compared with cervical cancer protection\(^*\) should be reconsidered in light of new epidemiological evidence on OSPCC. Reliance on data for anogenital malignancy has led to the vaccines' potential benefits for disease prevention being underestimated. Morbidity and mortality from oropharyngeal cancer are vital missing parts of the data in this debate.

Andrew G Schache Wellcome Trust-FDSRCS research training fellow, Department of Molecular and Clinical Cancer Medicine, Institute of Translational Medicine, University of Liverpool, Liverpool L69 3GQ, UK. schache@liverpool.ac.uk

Richard Simonck consultant clinical oncologist

Duncan C Gilbert consultant clinical oncologist, Sussex Cancer Centre, Royal Sussex County Hospital, Brighton, UK

Richard J Shaw clinical senior lecturer in head and neck surgery, Department of Molecular and Clinical Cancer Medicine, Institute of Translational Medicine, University of Liverpool, Liverpool L69 3GQ, UK

Competing interests: None declared.


Cite this as: BMJ 2011;343:d6675

### CERVICAL SCREENING IN UNDER 25s

**Dr McCartney is right, the BMA is wrong**

We agree with McCartney and fully support the English policy of not doing cervical smears in women under 25.\(^*\) Treating lesions that were destined for spontaneous regression can cause lasting harm to young women and is wrong. All the referenced studies she cites reiterate this.

Young women with symptoms such as intermenstrual or postcoital bleeding should be screened for infection and, if necessary, treated in general practice; if symptoms continue they should be referred to gynaecology. Doing a smear is not appropriate. The policies of Wales, Scotland, and Northern Ireland to screen from age 20 are misguided. Why are these countries free to ignore evidence based medicine, waste money, harm young women, and foster an impression that England is denying lifesaving screening?

Also embarrassing to us, as BMA members, is the BMA 2009 ARM motion that was carried after a few minutes’ debate: “This meeting strongly recommends to the Department of Health Advisory Board that the lower age limit for screening should be 20.” This is no way to formulate policy on a highly technical and emotive issue. We urge the BMA to retract that resolution. We also hope the other nations have the courage to follow the evidence, change to first smear at 25, and ride out the ensuing tabloid beatings. As McCartney concluded it is the “right thing” to do.

Colm P O’Mahony consultant in sexual health and HIV, Countess of Chester NHS Trust, Chester CH2 1UL, UK

Angela Robinson consultant in sexual health and HIV, Camden Primary Care Trust, London, UK

Simon Barton director sexual health and HIV, Chelsea and Westminster Trust, London, UK

Bill Beeby general practitioner, Parkway Medical Centre, Middlesbrough, UK

Competing interests: None declared.

1 McCartney M. GMtY’s Dr Steele is wrong to promote cervical screening in under 25s. BMJ 2011;343:d6167. (28 September.)

Cite this as: BMJ 2011;343:d6679

### SUSPECTED EARLY DEMENTIA

**Imaging those with cognitive impairment is not practical**

As Schott and colleagues state,\(^*\) UK, European, and US guidelines recommend that all patients with cognitive impairment should undergo structural imaging, and as good modern doctors we follow these guidelines, slavishly. We have been doing computed tomography scans on these patients for 15 years. We have been requested to scan a 101 year old with memory loss. We have found the occasional asymptomatic meningioma but no relevant brain tumour and no hydrocephalus or haematoma.

The best we can achieve, as in the case quoted in the article, is to label the patient, more or less accurately, with the particular form of dementia he or she may have. In the absence of disease modifying treatment, this achieves virtually nothing in practical terms. It merely consumes valuable imaging resources at a time of increasing financial restriction.

This article is intellectually interesting, but has made a negative contribution to the rational use of imaging.

David M Hill consultant radiologist, NHS Dumfries and Galloway, Dumfries DG1 4TG, UK dhill@btinternet.com

1 Schott JM, Warren JD, Barkhof F, Rossor MN, Fox NC. Suspected early dementia. BMJ 2011;343:d5568. (20 September.)

Cite this as: BMJ 2011;343:d6650

### ISSUES AROUND EARLY DIAGNOSIS OF ALZHEIMER’S DISEASE

**Authors’ reply to HESTeria or hype?**

In reply to Scott and colleagues,\(^*\) we found an unequivocally wide variation in reappearance after colorectal surgery. Furthermore, variation is identifiable at high surgical caseloads, through techniques such as neuroimaging\(^*\) because diagnosis of dementia is often delayed. "AD" is often used interchangeably for Alzheimer’s disease and Alzheimer's dementia, which risks the two imperatives becoming confused.

Recent research found that 43% of cognitively intact patients (mean age 83.7 years at death) had Alzheimer's disease at necropsy.\(^*\) Worldwide epidemiological follow-up studies showed that the rates of transition between the earliest detectable memory loss and Alzheimer's dementia is around 33-50% over three years for the type of memory loss considered most likely to be "pre-Alzheimer’s."\(^*\) These findings suggest a large potential for false positive diagnoses of Alzheimer’s disease.

A correct early diagnosis of Alzheimer's disease could be valuable since it allows informed planning for the future. However, the consequences in falsely diagnosed cases could be grave. Conferring a diagnostic label is far from neutral, and doctors must consider whether the earliest possible diagnosis of Alzheimer's disease might result in an increased risk of suicide.

Furthermore, knowledge is almost non-existent on how patients might react to such a diagnosis long before dementia may or may not develop.\(^*\) Research seems to point to large numbers of people with early memory loss not developing dementia. As we learn to identify risk, we need to do so in a way that is more likely to benefit than harm patients.

Peter J Gordon consultant old age psychiatrist, Clackmannann Community Healthcare Centre, Sauchie, Alloa, Clackmannanshire FK10 3Q, UK. petergordon@nhs.net

Sian F Gordon general practitioner, Graeme Medical Centre, Falkirk, Stirlingshire FK7 7HR, UK

Competing interests: None declared.


2 Schott JM, Warren JD, Barkhof F, Rossor MN, Fox NC. Suspected early dementia. BMJ 2011;343:d5568. (20 September.)


Cite this as: BMJ 2011;343:d6613

### COLORECTAL SURGERY PERFORMANCE

*Authors’ reply to HESTeria or hype?*
sustaining that centralisation of surgical services, a policy commonly applied to reduce variation, may be ineffective. Our duty as researchers is to report variation when it clearly exceeds what would be expected by chance. The extent to which variation in reoperation, as measured by our proposed metric, reflects genuine differences in quality requires substantiation. These findings should therefore be regarded as the starting point rather than the final story.

The strengths and weaknesses of Hospital Episode Statistics (HES) are well documented. Scott and colleagues propose a bespoke morbidity reporting system as an alternative, but this may not necessarily be superior. In a recent national comparison of HES with voluntarily reported National Bowel Cancer Audit Project (NBOCAP) data, we identified more surgical cases and higher national 30 day mortality with HES. This questions the validity of using voluntary datasets for national performance benchmarking.

Cost considerations are also important. Expense is estimated to be £1 per record for HES and up to £60 for clinical registry records. Most importantly, however, HES is currently the only comprehensive English national dataset. It is no accident therefore that leading surgical outcomes research, including studies carried out by the Royal College of Surgeons, use this important data resource despite its accepted limitations.

Reoperation for complications is important to patients and healthcare providers for the obvious human and financial costs incurred. Thus wide variation will concern the public and journalists. Many surgeons think that professional credibility seeks to improve surgical performance must be nothing to hide. Research that questions and variation will concern the public and journalists.

The meta-analysis by Wiesenauer and Luedtke included eight randomised controlled trials (RCTs). A re-analysis of the four published placebo controlled RCTs revealed serious flaws, including non-validated outcome measures, all the studies originating from Wiesenauer’s own group, and a lack of independent replication. Furthermore, relatively low dilutions were used, which contain active molecules and generate pharmacological effects contrary to ultra-molecular dilutions.

Taylor et al pooled the data from their own four RCTs and found a mean symptom reduction of 28% in the experimental group and 3% in the placebo group. This article has been criticised repeatedly. A placebo response as low as 3% is puzzling (around 30% would be typical). A meta-analysis of the authors’ own studies can hardly be convincing. Moreover, these were not of homoeopathic remedies relying on the “like cures like principle” but of isopathy, which is based on using causative agents.

The health technology assessment by Bornhoeft et al included weak evidence such as uncontrolled studies. In the “strongest” domain of upper respiratory tract infections, it included 16 placebo controlled trials, eight of which were positive. This unconvincing evidence also lacked critical input and included many studies of low dilutions.

Bellavite et al state “whether homeopathic high dilutions are placebos... is still a matter of debate... A general weakness of evidence derives from lack of independent confirmation of reported trials and from presence of conflicting results” Witt et al evaluated 67 in vitro experiments and discovered that “nearly three quarters of them found a high potency effect. Yet they had to concede that “no positive result was stable enough to be reproduced by all investigators.” Thus, this best case for homeopathy is fundamentally flawed and hopelessly weak. If evidence of efficacy as poor as this was offered for registration of a new drug, it would not succeed.
Competing interests: All the authors belong to Healthwatch-UK (www.healthwatch-uk.org.uk), a charity that promotes evidence-based treatment. NR is the president of Healthwatch and a trustee of Sense About Science, which promotes, well, sense about science. As previously stated.


4 Miller B. Statistics in study were flawed. BMJ 2000;322:169.

5 Brown HM. Did patients really have allergic rhinitis? BMJ 2000;322:170-1.

6 Windeler J. Results of study were not convincing in favour of homeopathy. BMJ 2000;322:170.


Cite this as: BMJ 2011;343:d6693

Bewley and colleagues’ quotation of review is selective

Bewley and colleagues (previous letter) quote two sentences from the abstract of my review: “whether homeopathic high dilutions are placebos . . . is still a matter of debate . . . A general weakness of evidence derives from lack of independent confirmation of reported trials and from presence of conflicting results”.

This citation cannot be used to support their negative view for three reasons: (a) in the paper I extensively explain that the placebo question in complex interventions such as homeopathy must be kept separate from the question of clinical effectiveness for technical and conceptual reasons; (b) weakness of evidence does not mean absence of evidence, neither is it proof of lack of efficacy; and (c) the authors have omitted the words that in my abstract lie between the two sentences that they report.

The words omitted by Bewley and colleagues after debate are: “The evidence demonstrates that in some conditions homeopathy shows significant promise, eg Galphimia glauca (low dilutions/potencies) in allergic ocularitis, classical individualized homeopathy in otitis and possibly in asthma and allergic complaints, and a few low-potency homeopathic complexes in sinusitis and rhinoconjunctivitis.” A recent systematic review from my research group confirmed and updated this evidence.1

Paolo Bellavite professor of general pathology, University of Verona, Verona, Italy paolo.bellavite@unjur.it

Competing interests: None declared.


PFI CAUSING FINANCIAL PROBLEMS

NHS cuts and PFI

Lansley suggests that the private finance initiative (PFI) is the main cause of financial problems among 22 NHS trusts, which are “on the brink of collapse.”2 The media have largely reflected the line that Lansley is faced with the task of cleaning up Labour’s “mess,” and that any hospital closures he sanctions can be blamed on them.

This account is misleading. The destabilising influence of PFI within the context of payment by results has long been understood. Because payment by results allocates resources to trusts on the basis of average treatment costs across the NHS, trusts with PFI projects in place (and therefore much higher than average fixed costs) will often run deficits. Such deficits accumulate over time and can become unmanageable.

The question is what we should do about this. It serves no efficiency purpose to penalise trusts for having high fixed costs, which are ultimately traceable to decisions taken in Whitehall. It is not surprising that the current government has embraced this form of off-balance sheet financing. But it should clearly state that it has done so and stop playing politics.

Mark Hellowell lecturer, Global Public Health Unit, School of Social and Political Science, University of Edinburgh, Edinburgh EH9 9LD, UK mark.hellowell@ed.ac.uk

Competing interests: None declared.

1 O’Dowd A. Trusts deny health secretary’s claims that private finance initiatives have caused major financial problems. BMJ 2011;343:d6133. (26 September.)

Cite this as: BMJ 2011;343:d6681

HEALTH INFORMATION FOR ALL

Language is essential for access to information

Language is key to accessing information.1 Speakers of a dominant language such as English—including most highly educated professionals in developing countries—may easily overlook the fact that the people who most need healthcare information are not likely to have a good understanding of English (or of French, Spanish, or Portuguese).

Language is a large obstacle to comprehension, whether training community healthcare workers with varying levels of education or delivering information to the end consumers—often people in rural communities.

Ironically, people with scant knowledge of English tend to be those who need access to information the most. In the case of Africa, with 25% of the world’s disease burden and only 2-3% of its doctors and nurses, well informed healthcare workers are crucial. If, however, neither the people themselves nor the village healthcare workers meant to help them have strong English skills, the information they have access to will be understood imperfectly or not at all. The whole chain of access to information breaks down.

Lori Thicke founder, Translators without Borders, 75011 Paris, France lori@translatorswithoutborders.org

Competing interests: None declared.

1 Smith R, Koelmools TP. Provision of health information for all. BMJ 2011;342:d4451. (30 June.)

Cite this as: BMJ 2011;343:d6253