Obama's giant step towards universal health insurance

The health reform bill extends insurance to 31 million Americans

SIPA PRESS/REX FEATURES

FEATURE, p 680, NEWS, p 671

Gavin Yamey lead, Evidence to Policy Initiative, Global Health Group, University of California San Francisco, 50 Beale Street, Suite 1200, Box 1224, CA 94105, USA
yameyg@globalhealth.ucsf.edu

Competing interests: GY volunteered for, and donated to, Barack Obama's 2008 presidential campaign, and donated to the congressional campaigns of several Democrats. He is a member of Organizing for America, a community organising project of the Democratic National Committee, and of Planned Parenthood, a sexual and reproductive healthcare provider and advocacy organisation. He receives employer based health insurance from the University of California San Francisco.

Provenance and peer review: Commissioned; not externally peer reviewed.

Cite this as: *BMJ* 2010;340:c1674
doi: 10.1136/bmj.c1674

In 1912, Theodore Roosevelt, the 26th president of the United States (1901-9), formed the short lived Progressive Party, which campaigned on a promise of national health insurance. "What Germany has done in the way of old age pensions or insurance," he said "should be studied by us, and the system adapted to our uses."[1] So began the story of successive American presidents trying and failing to achieve comprehensive health reform. On Sunday 21 March 2010, at 10.45 pm in Washington, DC, after a year of rising and falling political fortunes, Barack Obama, the 44th president, brought the story to an end with the passage of a bill that achieves near universal health insurance. The bill will be his legacy.

Three policy imperatives shaped the landmark legislation. The first was to expand health insurance coverage. The US is the only major industrialised nation that fails to guarantee coverage for all its citizens.[2] More than 46 million Americans are uninsured, and a recent study estimated that about 45 000 deaths per year are associated with lack of insurance.[3 4] The second was to end the unfair practices of the private health insurance industry, such as denying coverage to anyone with a "pre-existing medical condition" or rescinding coverage when a patient gets ill. The third was to curb the spiralling costs of health care, which were threatening to explode the federal budget.

Tackling these policy imperatives was a huge challenge because it meant spending money to expand insurance while simultaneously making savings. Although far from perfect, the Patient Protection and Affordable Care Act,[5] due to be signed into law on 23 March, is a giant step towards meeting this challenge. It will be further improved if the Senate passes an additional package of fixes (Reconciliation Act 2010) that has already passed the House.

The bill represents "comprehensive reform with an incremental soul."[6] Although it will expand coverage to 31 million uninsured Americans by 2019, tackling the first policy imperative, it does so largely by preserving the existing private insurance system. From 2014, nearly all US citizens and legal residents are mandated to have health insurance or else pay a penalty. Individuals and employers will be able to shop for insurance through new online exchanges—the key innovation in the bill—where they can compare the prices, benefits, and consumer rated quality of different plans. People on low and middle incomes will receive generous subsidies to purchase a plan, and small businesses will be given tax credits to buy insurance for their employees. Large businesses that refuse to offer employer based insurance will pay a penalty. Insurance coverage will also be expanded by widening the eligibility criteria for Medicaid, the social insurance programme for people on very low incomes.

The bill tackles the second imperative through far reaching regulations on the insurance industry. Within six months of enactment, it will be illegal for insurers to deny coverage to children on the basis of pre-existing conditions or to rescind coverage when a person becomes ill or injured. Once the exchanges become operational in 2014, the ban on discriminating against people with pre-existing conditions will apply to everyone.

Finally, the bill makes inroads into cost control (see box on bmj.com). It more than pays for itself, partly through new taxes on high cost insurance plans and on wealthy Americans. The non-partisan Congressional Budget Office estimates that the bill will reduce the federal budget deficit by $118bn (£78bn; €87bn) in the next 10 years.[7] Healthcare quality experts are encouraged by the bill's support for comparative effectiveness research tied with pilot studies in Medicare, the social insurance programme for people aged 65 and over. These pilots will test ways of paying providers on the basis of the quality and not the quantity of care.

The biggest winners will be the working poor, who currently fall through the cracks of the welfare system. They have jobs, but their employers don't offer insurance. They earn a little too much to qualify for Medicaid and are too young for Medicare. Their wages are too low for them to afford the exorbitant costs of health insurance in the individual marketplace. The bill gives them subsidised access to insurance for the first time.

The bill will have a smaller effect on people who already have insurance through their employer, although it will give them peace of mind. From 2014, if they lose their job they will be able to purchase a plan on the insurance exchanges, regardless of any pre-existing condition, and will receive subsidies based on a means test.

This is the most important social legislation since the 1965 creation of Medicare and Medicaid. Many had hoped for more radical reforms, such as the option for people under 65 to buy into Medicare ("Medicare for all"), or the inclusion in the exchanges of an insurance plan run by the government (a "public option"). But there were not enough votes in the Senate to pass such reforms. The bill represents what was politically possible.

Of the many shortcomings in the bill, two are particularly troubling. Firstly, proof of citizenship is required to purchase insurance on the exchange, leaving at least 5.6 million undocumented immigrants uninsured,[8] which is an affront to the notion of health care as a fundamental human right. Secondly, women on low incomes who receive federal subsidies to buy insurance on the exchanges are barred from using them to pay for an abortion, which arguably curtails poor women's reproductive rights.[9]

Despite these caveats, the bill should be celebrated for moving America's health system in the right direction, by extending insurance to 94% of US residents.[10] It begins a process of reform that can be improved on over time. It rejects Ronald

Reagan's claim that government is the problem, reasserting the notion that government can provide solutions to our big challenges. The bill is a triumph of compassion towards the uninsured over the fear mongering stoked by President Obama's Republican opponents. As such, it is already being talked about as "the civil rights act of the 21st century."[11]

1 Roosevelt T. Roosevelt's own creed set forth. *New York Times* 1912 August 7.
2 Davis K. Universal coverage in the United States: lessons from experience of the 20th century. *J Urban Health* 2001;78:46-58.
3 Kaiser Family Foundation. Health insurance coverage in America 2008. 2009. www.kff.org/uninsured/7995.cfm.
4 Wilper AP, Woolhandler S, Lasser KE, McCormick D, Bor DH, Himmelstein DU. Health insurance and mortality in US adults. *Am J Public Health* 2009;99:2289-95.
5 Democratic Party Committee. The Patient Protection and Affordable Care Act. http://dpc.senate.gov/dpcdoc-sen_health_care_bill.cfm.
6 Klein E. A bill becomes a law. *Washington Post* 2010 March 22. http://voices.washingtonpost.com/ezra-klein/2010/03/a_bill_becomes_a_law.html.
7 Congressional Budget Office. Estimate of the budgetary effects of the senate-passed health bill. http://cboblog.cbo.gov/?p=488.
8 National Institute for Health Care Management. Understanding the uninsured: tailoring policy solutions for different subpopulations. NIHCM Foundation issue brief. 2008. www.nihcm.org/pdf/NIHCM-Uninsured-Final.pdf.
9 NARAL Pro-Choice America. Statement on health reform. 2010. www.prochoiceamerica.org/news/press-releases/2010/pr03212010-finalhousehcr.html
10 Trust for America's Health. http://healthyamericans.org/assets/files/PatientProtectionShortSummary.pdf.
11 Pear R, Herszenhorn DM. Obama hails vote on health care as answering the "call of history." *New York Times* 2010 March 21. www.nytimes.com/2010/03/22/health/policy/22health.html.

Reducing sunbed use in young people

Does this require legislation or voluntary regulation?

JUSSI NUKARI/REX FEATURES

RESEARCH, p 694

J Mark Elwood vice president, Family and Community Oncology, British Columbia Cancer Agency, Vancouver, BC, Canada V5Z 1G1
melwood@bccancer.bc.ca
Richard P Gallagher head, Cancer Control Research, British Columbia Cancer Agency, Vancouver, BC, Canada V5Z 1L3

Cite this as: *BMJ* 2010;340:c990
doi: 10.1136/bmj.c990

In the linked study, Thomson and colleagues report two related surveys in England (with some data from Scotland and Wales) on the use of sunbeds by young people.[1] In the national English survey, the prevalence of "ever use" of a sunbed rose from 1.8% at age 11-14 to 11.2% at age 15-17, and it was higher in girls, in the north of England, and in lower socioeconomic groups, reaching around 50% in older girls in some cities. About half the users had used a sunbed within the past month so may be regular users. This is the largest such survey in Britain, but no information on skin type or ethnic background was given. These prevalence figures are lower than those from some other European countries, the United States, and Australia, but they are still substantial and may be increasing. The authors are unequivocal in calling for legislation to outlaw the use of sunbeds by those under 18 and to ban coin operated and unstaffed outlets.

Why would anyone want to be "slow roasted as the filling in a sunbed sandwich"?[2] Because sun tanned skin is desirable for many young people; its cosmetic and psychological benefits are widely accepted, and many people consider artificial tanning safer than exposure to the sun. These attitudes reflect strong industry advertising, with an emphasis on the value of vitamin D and the protective value of building up a preholiday tan[3 4]; franchise managers advertise, "Fun atmosphere, easy to operate, huge profit margins."[5]

In this study, 42% of non-users gave health risks as a reason for their choice. The increased risk of melanoma is accepted by international groups such as the World Health Organization. The estimated relative risk is not high—only 1.15 for ever use but 1.75 for first sunbed use before age 35 years.[6] These risks are not clearly greater than the risk of melanoma conferred by intermittent sun exposure through holidays and recreation,[7] although all these risks will be underestimated because of the inaccuracy of the exposure information and the limited duration of time since exposure in many studies. Evidence for increased squamous cell or basal cell cancers is less consistent.

Tanning beds emit ultraviolet A radiation and some ultraviolet B. The intensity of ultraviolet A may be many times higher than the midday sun, so it is an exposure that is not found naturally and may have unknown effects.[8] Ten to 20 hours a year of such exposure may exceed a person's annual exposure to ultraviolet light from the sun.[8] Sunbeds are poorly controlled. A European study showed that many of the sunbeds tested had ultraviolet light intensities over the recommended limit of 0.3 W/m, with the highest being nearly five times that limit.[9] A survey from Northern Ireland showed that the type of ultraviolet light used was unknown in 71% of sunbed premises.[10] The use of sunbeds is also associated with several acute ill effects, from erythema to photodrug reactions and mitochondrial changes associated with photoageing.

The use of sunbeds may seem a modest risk compared with other hazards in adolescence, such as smoking, alcohol and drug misuse, obesity, dangerous driving, and so on, although the risk of cancer may rise as follow-up times increase. But as a minimum requirement, access to or the sale of sunbeds needs to be accompanied by responsible and accurate information on the hazards, to inform consumers' rights. This is not happening. In this survey, many users were not given information about the potential harms of sunbeds. Furthermore, substantial numbers had used a sunbed at home or in an unsupervised facility. Recently, the operator of a coin operated suntan facility in Wales was convicted under health and safety laws after a 14 year old girl received severe burns; the judge likened the unsupervised tanning facility to an "unmanned, unsupervised off licence."[11]

Would responsible voluntary practices be adequate? The British industry group, the Sunbed Association, states that no member of their association would allow anyone under 16 to use their sunbeds. Australia has had a voluntary code of practice since 2002, which requires operators to ban access by those under 18 and people of any age who have skin type 1 (skin that does not tan). However, a survey there showed that sunbed use was offered to "shadow shoppers" aged 16 by more than half the facilities and to adults with skin type 1 by 90%; 14% of centres gave inadequate or no eye protection, and 75% reassured potential clients about the benefits versus risks of sunbeds.[12]

Short of an outright ban, parental permission can be required. Thirty one states in the US currently regulate access to tanning facilities by young people, with nine states banning access under age 14 and two more under age 16 or 16.5.[13] In a large US survey, 93% of suntanning facilities asked for parental consent in states that required such consent, but so did 76% of facilities in states without this requirement. At that time, only one state had a complete ban on access for under 16s, and even there 30% of facilities granted such access, although this was compared with 97%

in states without such a ban.[14] So enforcement, rather than voluntary codes of practice, is probably needed if behaviour is to be changed.

Legislative bans on giving young people access to tanning facilities have been recommended by WHO and many other groups, including an all party parliamentary group. France banned use by under 18s in 1997. Recent European Union regulations state that those under 18 should not have access to sunbeds. In Scotland, use by those under 18 was banned in 2008, with a requirement for operators to provide information on health risks. Proposals for similar actions in other parts of the United Kingdom seem well supported.

1 Thomson CS, Woolnough S, Wickenden M, Hiom S, Twelves CJ. Sunbed use in children aged 11-17 in England: face to face quota sampling surveys in the National Prevalence Study and Six Cities Study. *BMJ* 2010;340:c877.
2 Bailey A. Cranking up the heat on sunbed use. *Br J Nurs* 2008;17:621.
3 Indoor Tanning Association. Positive effects of UV light. 2005 www.theita.com/indoor/positiveeffects_ofUV.cfm.
4 Fabutan Sun Tan Studios. Be sun smart while you are away. 2010. www.fabutan.com/tanning-responsibly/pre-vacation-checklist.aspx.
5 Image Sun Tanning Centers. Fun atmosphere! Easy to operate! Huge profit margins. 2010. www.imagesun.com/request_info.shtml?gclid=CLio8qaVu58CFRKiagodlEs_zw.
6 International Agency for Research on Cancer, Working Group on artificial ultraviolet light and skin cancer. The association of use of sunbeds with cutaneous malignant melanoma and other skin cancers: a systematic review. *Int J Cancer* 2007;120:1116-22.
7 International Agency for Research on Cancer. IARC monographs on the evaluation of carcinogenic risks to humans. Solar and ultraviolet radiation. 2004.
8 Autier P. Perspectives in melanoma prevention: the case of sunbeds. *Eur J Cancer* 2004;40:2367-76.
9 Product Safety Enforcement Forum of Europe (PROSAFE). Press Release. 2009. www.prosafe.org/read_write/File/Press-Releases/Sun%20Beds-%20concluding%20press%20release.pdf.
10 Gavin A, Donnelly C, Devlin A, Devereux C, O'Callaghan G, McElwee G, et al. Public at risk: a survey of sunbed parlour operating practices in Northern Ireland. *Br J Dermatol* 2009. Published online 18 November.
11 Sunbed salon owner admits breaches of safety rules. *Western Mail* 2009. www.allbusiness.com/legal/trial-procedure-magistrates/13544192-1.html.
12 Dobbinson SJ, Sambell N, Wakefield MA. Access to commercial indoor tanning facilities by adults with highly sensitive skin and by under-age youth: compliance tests at solarium centres in Melbourne, Australia. *Eur J Cancer Prev* 2008;15:424-30.
13 National Conference of State Legislatures (NCSL). Tanning restrictions for minors: a state-by-state comparison. 2010. www.ncsl.org/IssuesResearch/Health/TanningRestrictionsforMinorsstatelawssummary/tabid/14394/Default.aspx.
14 Pichon LC, Mayer JA, Hoerster KD, Woodruff SI, Slymen DJ, Belch GE, et al. Youth access to artificial UV radiation exposure: practices of 3647 US indoor tanning facilities. *Arch Dermatol* 2009;145:997-1002.

Put Edward Jenner's statue back in Trafalgar Square

Hero who defeated an enemy of all humankind

Montage showing Jenner's statue restored to its original location in Trafalgar Square

Gareth Williams professor of medicine , Faculty of Medicine and Dentistry, University of Bristol, Learning and Research Building, Southmead Hospital, Bristol BS10 5NB
gareth.williams@bristol.ac.uk

Competing interests: Sales of his book, *Angel of Death: the Story of Smallpox*, could benefit from publication of this article but all royalties will be donated to the Edward Jenner Museum, Berkeley (www.jennermuseum.com).

Provenance and peer review: Commissioned; not externally peer reviewed.

Cite this as: *BMJ* 2010;340:c1582
doi: 10.1136/bmj.c1582

London's Trafalgar Square is famous for pigeons and statues of British military heroes. At its centre, Nelson presides from his column, celebrating the victory at Trafalgar that cost him his life but also set back Napoleon's ambitions to rule the world. At the corners of the square are four plinths, three of which carry statues.

A strikingly empty plinth awaits a final decision about what to put on it. Although recent occupants have included randomly selected people (with or without agendas, inhibitions, or clothes) the plinth began its career with pomp and circumstance, supporting an imposing statue unveiled in 1858 by Prince Albert and funded largely by public subscription.[1] The subject was an unconventional warrior who inspired loathing as well as adulation. His enemies were powerful—and four years later, his statue was quietly carted away and parked in obscurity in Kensington Gardens, where it remains today.

The statue is of Edward Jenner, widely known for developing a vaccine against smallpox. His "Inquiry," self published in 1798, contains the first documented cases of protection from smallpox after a previous infection with cowpox. Cowpox, caused by a poxvirus related to variolavirus, the smallpox virus, was a known occupational hazard in milkmaids. Jenner not only observed this remarkable lesson of nature but also translated it into practical treatment: he infected healthy subjects with cowpox and tested some by scratching smallpox pus into their skin—so called "variolation"—an established but intrinsically risky procedure that protected against the natural disease. None of his variolated subjects developed signs of smallpox and Jenner concluded that cowpox inoculation conferred immunity against smallpox.[2]

The importance of Jenner's discovery was quickly realised. Vaccination was available in North America by 1800 and India by 1802, and literally travelled around the world by 1806, thanks to the Royal Philanthropic Expedition which carried the new technology to Spain's colonies.[1] Accolades for Jenner flooded in from across the globe, including a hand written letter and a diamond ring from "Marie" (Empress of Russia), reverential titles from North American Indian tribes, and cash from impoverished cities in India. And three years before Trafalgar, while locked in hostilities with England, Napoleon granted Jenner's request to free two English prisoners of war, saying "I can refuse this man nothing."[3]

Back in England, however, Jenner faced strong opposition. Wealthy "variolators," who fleeced patients by cloaking the procedure in lucrative mystery, fought to defend their income. Leading doctors, jealous or dismissive of the provincial surgeon, set out to undermine vaccination; some claimed that children developed cow-like features after vaccination.[4] Churchmen, appalled by people being infected with "bestial" pus, bent Biblical texts to prove that vaccination was the devil's invention. Posthumously, Jenner became the focus of anger stirred up by legislation making the vaccination of infants compulsory. The anti-vaccinationists were merciless in their criticism of Jenner—"His unscientific, foolish, unsupported assertions show that it was time that he should die"[5]—but had little to offer as an alternative. One "cure," published in 1884, recommended bleeding with leeches, which were applied to the anus in cases where a confluent rash left no normal skin.[6]

Jenner was not perfect. His scientific approach was more Brownian than Newtonian. An easily distracted procrastinator, he took more than 20 years from first discussing vaccination to trying it out. The "Inquiry" was full of holes.[7] He did not even state how many experimental subjects he studied and initially covered up the reason that one of his "guinea pigs" was unavailable for follow-up (the boy, inoculated with pus from blisters on a horse's heel rather than cowpox, died of a fever). Jenner was not the first to make the connection between an attack of cowpox and subsequent protection against smallpox. Moreover, others had already inoculated healthy subjects with cowpox as long as 20 years before his first experiments, notably Benjamin Jesty in Dorset and—uncomfortably close to

doc2doc.bmj.com
Should Jenner's statue be returned to Trafalgar Square? Follow the debate at doc2doc.bmj.com, the BMJ Group's global online clinical community

bmj.com podcast
For an interview with Gareth Williams listen at podcasts.bmj.com/bmj

home—Jenner's friend and colleague, John Fewster.[8] However, Jenner was the first to publish and disseminate his results, thus dragging vaccination into mainstream medical practice. Ultimately, vaccination was the decisive weapon that eradicated smallpox in 1978, nearly 180 years after Jenner voiced his aspiration that his invention would achieve that aim. Meanwhile, smallpox has also been eradicated from the world's consciousness. We have forgotten that this disease was one of the most brutal killers and mutilators in our history. Before vaccination, smallpox attacked one person in three and killed one in 12; even in the 20th century it killed 300 million people. Many survivors were left severely scarred or blinded.

Much has moved on since the Battle of Trafalgar. Our enemies then are our friends today (mostly), but the statues of long dead military men remind us that the freedoms we now take for granted were not won easily. On that basis, Jenner's statue deserves reinstatement alongside the other Trafalgar Square heroes. Napoleon's reign of terror lasted 20 years, while smallpox stalked the planet for centuries. In defeating smallpox, Jenner opened the door for immunisation against many other infections, and vaccination has proved to be one of medicine's most transferable technologies. To date, smallpox is the only infection that we have eradicated, but polio and other major killers will undoubtedly follow. A century from now, Jenner's legacy will be even stronger, whereas Nelson's may well have shrunk further into history.

The year 2010 is the 30th anniversary of the World Health Organization's formal declaration of the greatest public health coup of all time, the eradication of smallpox. This is a fitting time to recognise Jenner for his role in defeating an enemy of all humankind, not just of England, that killed more people than all human wars combined. A petition to persuade the government to restore Jenner's statue to its original and rightful place alongside the other heroes of Trafalgar Square can be accessed at http://petitions.number10.gov.uk/Jenner2010/.

1 *British Medical Journal*. Jenner Centenary issue. 23 May, 1896.
2 Jenner E. An inquiry into the causes and effects of the variolae vaccinae: a disease discovered in some of the western counties of England, particularly Gloucestershire, and known by the name of the cow pox. London: Sampson Low, 1798.
3 Baron J. *Life of Edward Jenner, MD with illustrations from his doctrines, and selections from his correspondence*. London: H Colbourn, 1827 (vol 1), 1838 (vol 2).
4 Rowley W. *Cox-pox inoculation no security against small-pox infection*. London: J Harris, 1805.
5 Wheeler A. Vaccination. Opposed to science and a disgrace to English law. An address delivered at Darlington, 10 November 1879. London: EW Allen, 1879.
6 Boëns H. *La variole, la vaccine et les vaccinides en 1884*. Reprinted from the *Bulletin de l'Académie Royale Médicale de Belgique*, vol 18, no 1. Brussels: A Manceaux, 1884.
7 Baxby D. Edward Jenner's Inquiry; a bicentenary analysis. *Vaccine* 1999;17:301-7.
8 Williams G. Everyday tales of country folk. In: *Angel of death: the story of smallpox*. Palgrave Macmillan, 2010:161-74.

The new CONSORT statement

The guidance is clear, but awareness and endorsement are lagging behind

RESEARCH, p 697
RESEARCH METHODS AND REPORTING, p 698

Gerd Antes scientist and director of German Cochrane Centre, German Cochrane Centre, Berliner Allee 29, 79110 Freiburg, Germany
antes@cochrane.de

Cite this as: *BMJ* 2010;340:c1432
doi: 10.1136/bmj.c1432

Full and transparent reporting of results of clinical trials is essential for assessing the quality of healthcare interventions. Inadequate reporting of trials is common, and it impedes the use of trial results in healthcare research and practice.[1] Consequently, during the past 15 years, a series of reporting guidelines have been developed and recently collected by the Equator Initiative (www.equator-network.org).[2] The pioneering first step of this framework was the CONSORT statement in 1996,[3] which provided recommendations for the publication of randomised controlled clinical trials, the gold standard to assess healthcare interventions. The 2010 update of the statement (doi:10.1136/bmj.c332)[4] is accompanied by a comparative study by Hopewell and colleagues,[5] which assesses whether the quality of reporting of randomised trials has improved since publication of the CONSORT statement in 2001.

Concerns have been raised that such publication guidelines may be too prescriptive, impede the creativity of research, and lack authorisation of the self selected author groups who write them.[6] However, these concerns are clearly outweighed by the harm caused by poor reporting. Thus, broad acceptance of CONSORT and other statements has been a natural step towards achieving better quality of trial reporting. That is the theory, but what about the practice?

Hopewell and colleagues compare the reporting characteristics and methodological details of randomised trials indexed in PubMed in 2000 and in 2006.[5] By looking at 616 trials indexed in December 2006, and a similar sample from 2000, they assessed whether the quality of reporting has improved since publication of the revised CONSORT statement in 2001.[3] Two key messages emerged: firstly, improvements occurred in the reporting of several items that are crucial for the assessment of trial quality; and secondly, these improvements generally started from an embarrassingly low level. Improving the quality of reporting from very poor to poor could be interpreted as a positive trend, but essential items like sample size estimation (27% *v* 45%), description of the randomisation procedure (21% *v* 34%), or description of the concealment of treatment allocation (18% *v* 25%) are described in an unacceptably low number of reports. An optimistic perspective would be to view the glass as half full; a realistic one would have to admit that the glass is more than half empty.

A look at the proportion of journals that support the CONSORT statement may help to gain more insight into these disappointing figures. Hopewell and colleagues showed that even among high impact journals, fewer than 50% recommend that authors comply with the CONSORT statement.[7 8] Of those, only a minority have procedures that support adherence to the requests from the CONSORT statement by authors and reviewers.[7]

So what has changed in the new update of the CONSORT statement? In addition to improvements of wording and consistency across items, several items were extended to include sub-items that concern, for example, allocation concealment, blinding, or other methodological matters. A few new items were introduced: registration is now required before inception, and researchers must state where the protocol can be accessed (if this is possible) and where the funding comes from.

Why is better endorsement and adherence to the CONSORT statement not achieved although the evidence of benefit is impressive?[9] The answer is unclear and therefore speculative.

Even after almost 15 years, the main reason seems to be the lack of awareness and a considerable amount of ignorance about recommendations like CONSORT. Journal editors have an essential role, and their reluctance may be based on the expectation of a serious increase in workload. However, much of the workload could be shifted to authors. Incorporating the CONSORT checklist into the peer review process might increase the workload of authors initially, but it would help to simplify and structure the review process by enabling reviewers to check trial reports against the CONSORT items. This would establish a solid communication structure between authors, reviewers, and editors, but this approach has not been implemented on a large scale so far. The simplest explanation for this may be mere lack of appreciation of the importance of publication ethics. This was confirmed by a survey of editors, which concluded that most editors of science journals are not very concerned about publication ethics and believe that misconduct occurs only rarely in their journals.[10]

Finally, a problem with research in this field is the almost complete restriction to articles in the English language. Several mechanisms, especially the pursuit of academic incentives and maximum promotion of trial results, has led to reduced publication in non-English journals.[11] The migration of original research publications into English may solve this problem eventually. However, this risks the danger of moving towards double standards of quality requirements. Although global knowledge is mostly exchanged in the English language, a large number of local non-English language journals remain beyond systematic empirical investigations of their quality and beyond the reach of publication guidelines.[12] CONSORT has been translated into 10 other languages (www.consort-statement.org/consort-statement/translations), but not much is known about endorsement and adherence in those areas.[13]

1 Dwan K, Altman DG, Arnaiz JA, Bloom J, Chan AW, Cronin E, et al. Systematic review of the empirical evidence of study publication bias and outcome reporting bias. *PLoS ONE* 2008;3:e3081.
2 Altman DG, Simera I, Hoey J, Moher D, Schulz K. EQUATOR: reporting guidelines for health research. *Lancet* 2008;371:1149-50.
3 Moher D, Schulz KF, Altman D. The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomized trials. *JAMA* 2001;285:1987-91.
4 Schulz KF, Altman DG, Moher D; for the CONSORT Group. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. *BMJ* 2010;340:c332.
5 Hopewell S, Dutton S, Yu L-M, Chan A-W, Altman DG. The quality of reports of randomised trials in 2000 and 2006: comparative study of articles indexed in PubMed. *BMJ* 2010;340:c723.
6 Potvin L. Strobe and the standardisation of scientific practice. *Int J Public Health* 2008;53:9-10.
7 Hopewell S, Altman DG, Moher D, Schulz KF. Endorsement of the CONSORT statement by high impact factor medical journals: a survey of journal editors and journal "Instructions to Authors." *Trials* 2008;9:20.
8 Meerpohl JJ, Wolff RF, Niemeyer CM, Antes G, von Elm E. Editorial policies of pediatric journals: survey of instructions for authors. *Arch Pediatr Adolesc Med* 2010;164:268-72.
9 Altman DG, Schulz KF, Moher D, Egger M, Davidoff F, Elbourne D, et al. The revised CONSORT statement for reporting randomized trials: explanation and elaboration. *Ann Intern Med* 2001;134:663-94.
10 Wager E, Fiack S, Graf C, Robinson A, Rowlands I. Science journal editors' views on publication ethics: results of an international survey. *J Med Ethics* 2009;35:348-53.
11 Galandi D, Schwarzer G, Antes G. The demise of the randomised controlled trial: bibliometric study of the German-language health care literature, 1948 to 2004. *BMC Med Res Methodol* 2006;6:30.
12 Ofori-Adjei D, Antes G, Tharyan P, Slade E, Tamber PS. Have online international medical journals made local journals obsolete? *PLoS Med* 2006;3:e359.
13 Matarese V. Relationship between quality and editorial leadership of biomedical research journals: a comparative study of Italian and UK journals. *PLoS ONE* 2008;3:e2512.

Monitoring HPV vaccination programmes

Trials of bivalent vaccine show no association with pregnancy loss, but ongoing surveillance is recommended

DR P MARAZZI/SPL

RESEARCH, p 696

Karen Canfell Sydney rotary research fellow, Cancer Epidemiology Research Unit, Cancer Council NSW, Sydney, 2011, Australia karenc@nswcc.org.au

Cite this as: *BMJ* 2010;340:c1666
doi: 10.1136/bmj.c1666

Vaccines based on human papillomavirus (HPV) types 16 and 18 virus-like particles (VLPs) are highly effective in preventing the development of HPV 16/18 related high grade cervical intraepithelial neoplasia (CIN2+) in HPV naive females. Gardasil (Merck) is a quadrivalent HPV 16/18/6/11 vaccine formulated with a proprietary aluminium adjuvant; and Cervarix (GlaxoSmithKline) is a bivalent HPV 16/18 vaccine incorporating a novel adjuvant, AS04. In the linked study, Wacholder and colleagues report a pooled analysis of data on pregnancy loss from two randomised controlled trials of Cervarix vaccine.[1]

The bivalent vaccine was licensed in the European Union in 2007[2] and approved by the Food and Drug Administration in the United States in October 2009,[3] and has been selected for use in the national public HPV vaccination programmes of the Netherlands and the United Kingdom. In the UK, vaccination started in September 2008, and at least 3.5 million doses have been administered.[4] In England, three dose coverage in 12-13 year old girls is estimated at 80%; catch-up to age 18 will be conducted over approximately two years, with recent three dose coverage reported as 32% in 17-18 year old females.[5]

Prophylactic VLP HPV vaccines do not contain live virus. A broad consensus exists among regulatory authorities that, although no evidence suggests that HPV vaccines confer additional risk during pregnancy, the safety of vaccinating pregnant women has not been established.[2-4] Thus, neither of the HPV vaccines are recommended for use in pregnancy or in women planning to become pregnant over the vaccination course. Vaccine trials have specifically contraindicated pregnant women, with participants asked to use contraception during the vaccination period, but nevertheless some women did conceive during or soon after vaccination.[1 6]

Wacholder and colleagues report a pooled analysis of data on pregnancy loss from two phase III randomised controlled trials of bivalent AS04 adjuvanted vaccine versus hepatitis A vaccine control. This post hoc analysis was requested by the data safety and monitoring board of one of the trials, the Costa Rica Vaccination Trial, after interim analysis from the other trial, the multicentre PATRICIA study, suggested an imbalance in rates of pregnancy loss between the two arms.[1]

Because no detailed mechanistic hypothesis about how HPV vaccination would increase the risk of pregnancy loss has been described, the period of interest between vaccination and conception could not be specified a priori. Therefore, the authors used statistical methods that allowed the comparison to be made between HPV vaccinated and

Competing interests: The author has completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declares: (1) No financial support for the submitted work from anyone other than her employer; (2) No financial relationships with commercial entities that might have an interest in the submitted work; (3) No spouse, partner, or children with relationships with commercial entities that might have an interest in the submitted work; (4) that she has collaborative research agreements with some of the authors of the linked paper; and that she attended an advisory meeting convened by Merck in Philadelphia USA (November 2009) but declined any honorariums or expenses.

Provenance and peer review: Commissioned; not externally peer reviewed.

control women over different periods between vaccination and conception, noting that the study was powered "to detect a moderate effect of the vaccine in subsets of pregnancies." Rates of total pregnancies and live births were similar in HPV vaccine and control arms, and overall rates of pregnancy loss were not significantly different between the arms. In a secondary descriptive analysis, the authors identified no significant differences between arms when each trial was considered separately (consistent with recent analysis of PATRICIA data[6]) or in subgroups defined according to the number of vaccine doses, maternal age, or gestational age at pregnancy loss. In the descriptive analysis, rates of pregnancy loss in women who became pregnant within three months of the last vaccine dose were 14.7% and 9.1% in HPV vaccinated and control women, respectively; but the difference was not significant. The authors conclude that the "HPV vaccine probably does not cause miscarriage" although they could not completely rule out an increased risk among pregnancies conceived within three months of vaccination.[1]

The data reported by Wacholder and colleagues were part of the information considered by the Global Advisory Committee on Vaccine Safety in mid-2009[7] and by an FDA advisory committee in deliberations that led to the US regulatory approval of the bivalent vaccine. The FDA noted, among other factors, that in analysis of the available data "the rate of spontaneous abortion in each group, including the Cervarix group, was consistent with background rates reported in the literature (9-21%)."[3] Nevertheless, it was concluded that, "imbalance in rates of spontaneous abortions met regulatory criteria for a safety signal"[3] (indicating the need for further investigation), and this led to a requirement that a postmarketing study be conducted to evaluate pregnancy outcomes. Both manufacturers maintain pregnancy registries in the US, and a registry has been configured by the UK Health Protection Agency to follow up women who have received HPV vaccine from 60 days before their last menstrual period or at any time during pregnancy.

Although it is difficult to establish pregnancy rates and outcomes outside the context of controlled trials, these registries do provide a mechanism for continued surveillance of pregnancy loss in relation to background population rates. A report of the manufacturer's two year postmarketing surveillance data for the quadrivalent vaccine recently concluded that observed rates of pregnancy loss in vaccinated women were no greater than in unexposed women.[8]

If there is a small adverse effect of HPV vaccination on reproductive outcomes in the period after vaccination, confirmation would require data on pregnancy outcomes in relatively large numbers of women. Several parallel approaches to safety research can be taken, including pooled analysis of data from trials of each HPV vaccine[9 10] and across all AS04 adjuvanted vaccines. Ongoing analysis of pooled data from randomised controlled trials will continue to be an important area of future research.

The safety aspects of HPV vaccination have been the subject of extensive public and media scrutiny. By design, routine ongoing vaccination programmes are targeted at young girls before the onset of sexual activity, an age at which they will gain maximum benefit from vaccination. It is important to emphasise to these girls and their parents that no evidence exists that vaccination will increase the likelihood of pregnancy loss when they do decide to have children. In fact, in this group HPV vaccination could improve pregnancy outcomes because it reduces the risk of high grade precancerous abnormalities. It has been estimated that if 80% vaccination coverage can be maintained in 12-13 year old girls, rates of CIN3 in women under 30 years in the UK will eventually be reduced by half.[11] Treatment for these abnormalities involves an increased risk of reproductive complications, potentially because of compromise of mechanical function in pregnancy after removal or ablation of part of the cervix.[12]

Any potential for a small adverse effect on reproduction is a particularly important concern for vaccination catch-up programmes, and applying the precautionary principle, sexually active women who are vaccinated should be advised to use contraception. The current study provides provisional reassurance that young women of reproductive age do not run a substantially increased risk of pregnancy loss after bivalent HPV vaccination, but a programme of ongoing surveillance seems prudent. A recent report by the UK Medicines and Healthcare Products Regulatory Agency, after administration of more than 3.5 million doses across the UK, found that "the balance of risks and benefits of Cervarix remains positive."[4] As shown by Wacholder and colleagues, the risks, as well as the benefits, of HPV vaccination remain the subject of active research. Ongoing surveillance and research are needed to provide continuing reassurance about the positive balance of risk to the millions of young females vaccinated against HPV.

1 Wacholder S, Chen BE, Wilcox A, Macones G, Gonzalez P, Befano B, et al; for the CVT group. Risk of miscarriage with bivalent vaccine against human papillomavirus (HPV) types 16 and 18: pooled analysis of two randomised controlled trials. *BMJ* 2010;340:c712.
2 European Medicines Agency. Cervarix European public assessment report. Revision 5. 2009. www.ema.europa.eu/humandocs/Humans/EPAR/cervarix/cervarix.htm.
3 US Food and Drug Administration: vaccines, blood and biologics. Cervarix. www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm186957.htm.
4 UK Medicines and Healthcare products Regulatory Agency. Suspected adverse reaction analysis. Cervarix human papillomavirus (HPV) vaccine. 2010. www.mhra.gov.uk/Safetyinformation/Generalsafetyinformationandadvice/Product-specificinformationandadvice/HumanpapillomavirusHPVvaccine/CON023340.
5 Health Protection Agency. Annual HPV vaccine uptake in England: 2008/09. 2010. www.dh.gov.uk/dr_consum_dh/groups/dh_digitalassets/@dh/@en/@ps/documents/digitalasset/dh_111676.pdf.
6 Paavonen J, Naud P, Salmeron J, Wheeler C, Chow SN, Apter D, et al. Efficacy of human papillomavirus (HPV)-16/18 AS04-adjuvanted vaccine against cervical infection and precancer caused by oncogenic HPV types (PATRICIA): final analysis of a double-blind, randomised study in young women. *Lancet* 2009;374:301-14.
7 WHO. Global Advisory Committee on Vaccine Safety, report of meeting held 17–18 June 2009. *Wkly Epidemiol Rec* 2009;32:325-32.
8 Dana A, Buchanan KM, Goss MA, Seminack MM, Shields KE, Korn S, et al. Pregnancy outcomes from the pregnancy registry of a human papillomavirus type 6/11/16/18 vaccine. *Obstet Gynecol* 2009;114:1170-8.
9 Garland SM, Ault KA, Gall SA, Paavonen J, Sings HL, Ciprero KL, et al. Pregnancy and infant outcomes in the clinical trials of a human papillomavirus type 6/11/16/18 vaccine: a combined analysis of five randomized controlled trials. *Obstet Gynecol* 2009;114:1179-88.
10 Descamps D, Hardt K, Spiessens B, Izurieta P, Verstraeten T, Breuer T, et al. Safety of human papillomavirus (HPV)-16/18 AS04-adjuvanted vaccine for cervical cancer prevention: a pooled analysis of 11 clinical trials. *Hum Vaccin* 2009;5:332-40.
11 Cuzick J, Castanon A, Sasieni P. Predicted impact of vaccination against human papillomavirus 16/18 on cancer incidence and cervical abnormalities in women aged 20-29 in the UK. *Br J Cancer* 2010;102:933-9.
12 Kyrgiou M, Koliopoulos G, Martin-Hirsch P, Arbyn M, Prendiville W, Paraskevaidis E. Obstetric outcomes after conservative treatment for intraepithelial or early invasive cervical lesions: systematic review and meta-analysis. *Lancet* 2006;367:489-98.