The experimental studies of the effects of chemical warfare agents conducted on thousands of British military personnel over several decades at the Porton Down facility in the United Kingdom have been an ongoing source of controversy regarding the scientific, ethical, and moral environment in which they took place.1 Concerns about effects on health increased following a coroner’s finding in 2004 of unlawful killing regarding the death of a Porton Down subject in 1953 after cutaneous application of a chemical warfare nerve agent in a non-therapeutic experiment. This finding understandably raised important questions about the longer term health of the 18,000 British veterans who took part in the Porton Down experiments.2 To investigate this, two linked studies have assessed whether the risks of cancer or mortality are higher in veterans who took part in tests compared with those who did not.3-4

Established in 1916 in response to the use of chemical warfare agents against British troops in the first world war, the Porton Down facility was later expanded because of the threat posed by Germany during the second world war; the use of chemical weapons by Iraq; and the later attacks by terrorists against civilians, such as the release of sarin in a subway in Tokyo in 1995. In response to increasing public concern, the UK Ministry of Defence commissioned an epidemiological study to investigate a range of health outcomes in the military personnel who took part in the Porton Down chemical weapon experiments.

More than half of the Porton Down veterans were exposed to known or probable human carcinogens, most commonly dermal exposure to sulphur mustard,5 so Carpenter and colleagues’ study on cancer morbidity is of considerable scientific and public interest. The authors found no significant differences in the overall incidence of cancer nor in the incidence of most cancer types in Porton Down veterans compared with non-veterans.3 Although a few subgroups had some isolated excesses of specific cancer types—such as excess of cancer of the trachea, bronchus, and lung in Porton Down veterans exposed to Lewisite—the lack of smoking data and the large number of analyses make it difficult to draw any firm conclusions about the causal nature of these few findings.

Venables and colleagues’ study of mortality reported a small excess of overall mortality in the Porton Down veteran group.4 However, this overall excess was mainly the result of excesses in non-cancer causes of death, such as deaths from infectious and parasitic diseases, circulatory diseases, genitourinary causes, and external causes. Some of these excess deaths are probably related to the longer period of service of Porton Down veterans compared with that of the comparison veteran group in the study, rather than to their involvement in the Porton Down experiments. Importantly, the authors found no increase in cancer mortality, consistent with the main finding in the cancer morbidity paper.5

The authors acknowledge that their studies have some limitations. Because UK cancer data have been available only since 1971, cancer rates in the early years of the Porton Down programme could not be studied. Also, it was not possible to adjust their findings for important confounders, such as cigarette smoking. One of the major strengths of these studies was the painstaking and time-consuming attention to detail in the assessment of exposure, which is not easy when extracting data from records that are several decades old.6

The overall findings are consistent with other studies of veterans with short term or intermittent exposure to chemical weapons. These include the study of US navy veterans from the second world war, who participated in mustard gas chamber tests, which found no excess in any cause specific mortality.7 Also, the mortality study of US army Gulf war veterans who were potentially exposed to nerve agents during the March 1991 chemical weapons demolition at Kharnisya in Iraq, reported no significant findings, apart from a borderline excess of deaths from brain tumours.8

The findings of the two studies should provide some reassurance to Porton Down veterans and their supporters that they have no excess risk of cancer or major causes of death. Although human carcinogens such as sulphur mustard and benzene were used in the Porton Down experiments, it should be remembered that the level and duration of exposure are important determinants of future cancer risk. In this study, the veterans took part in the experiments for only one to four weeks, for an average of two days a week. Therefore, the cumulative doses received were probably small compared with industrial exposure in manufacturing facilities, and—as the studies found—too low to cause a measurable excess of cancer.

Although these findings are reassuring for cancer and mortality outcomes, we need to take a more global view of the health of Porton Down subjects. This research group has previously published results for some other outcomes, which—although they have some methodological limitations—showed excess reporting of symptoms and poorer quality of life in a subgroup of Porton Down veterans.9 The finding of excess symp-
toms has some similarities with reported effects in many other veteran groups after deployment to areas of high personal threat.\(^1\) Although the nature of the threat to Porton Down veterans was different from that experienced by other veterans, non-fatal and non-cancer health outcomes in Porton Down veterans remain an important area of future research and public interest.


interesting to know if this was the questionnaire as such or the explicit unambiguous questions asked about their condition, which could easily be incorporated into the general practitioner’s history taking. General practitioners were at best ambivalent about the questionnaire, and they often used their professional judgment rather than the results of the questionnaire to guide management. Again, it would be interesting to know if this was related to the nature of the questionnaires or the fact that they were less robust than had been assumed. The hospital anxiety and depression score for instance is designed to identify possible depression but further assessment is needed to confirm the diagnosis. This confirmation could possibly come from the general practitioners’ professional judgment.

General practitioners prescribe treatment that is not always in accordance with guidelines or with the QOF system. These studies provide evidence that patients’ needs are better assessed by general practitioners’ professional judgment than by guided care. The two linked studies did not look at the course of the patients’ depression, however, so we do not know how well the patients fared. Further analysis of general practitioners’ experience is therefore warranted for a more robust analysis of the QOF.

### Tocolytics and preterm labour

Whether to treat or not is the real dilemma, not which drug to use

Preterm labour is still the main cause of perinatal morbidity and mortality in the developed world. Despite a better understanding of the pathophysiology, and the recognition that it is a syndrome with multiple causes, rates continue to rise.1 In the linked cohort study, de Heus and colleagues assess the incidence of serious maternal complications with the use of tocolytic drugs for the treatment of preterm labour.2 Corticosteroids given to women at risk of preterm birth increase fetal lung maturity and can reduce fetal death, intraventricular haemorrhage, and respiratory distress by up to 50%.3 In contrast, it is still unclear whether tocolysis improves neonatal or longer term outcomes.4 Thus, the Royal College of Obstetricians and Gynaecologists’ clinical guideline on tocolysis concludes that, “it is reasonable not to use tocolytic drugs.”5

Despite the lack of evidence, several tocolytic drugs are commonly used worldwide. They are used primarily to delay delivery for up to 48 hours to allow for administration of corticosteroids or transfer to a unit with neonatal intensive care facilities (or both). Little consensus exists as to which tocolytic agent is the best. Beta agonists, atosiban, and indometacin all reduce the incidence of delivery within 48 hours compared with placebo, but none has been shown to improve neonatal outcomes.4 Nifedipine has not been studied in placebo controlled trials, but it is more effective at delaying delivery than beta agonists, and has been associated with improved neonatal outcomes.4 Atosiban and nifedipine have not been directly compared.

The study by de Heus and colleagues assesses maternal safety. They recorded adverse maternal effects in an unselected population of 1920 consecutive women given tocolytic drugs in routine clinical settings in the Netherlands and Belgium over an 18 month period. The most commonly used agent was atosiban (42%), followed by nifedipine (34%), beta agonists (14%), and indometacin (8%).

The overall incidence of adverse effects was reassuringly low, but the study highlights the dangers of multi-drug regimens, which have no proven benefit either sequentially or in combination. Four women needed intensive care after being subjected to such regimens—three of which included beta agonists. But before such practices are condemned outright, a thorough analysis of each case is warranted, so that further research into safer combination treatments is not compromised.

Because of the definitions used in the study design, postpartum haemorrhage was not included as a maternal adverse event. Some people may think this a surprising omission considering the basic mechanism of action of all tocolytics.

Consistent with previous studies, the beta agonists had a higher incidence of serious adverse drug reactions (1.7%) than nifedipine (0.9%); no such reactions were reported for atosiban. Hypotension was the most serious adverse drug reaction associated with nifedipine, which is not surprising.
Environmental waste in health care
Must be reduced for the overall carbon reduction strategy to succeed

In the linked analysis article, Hutchins and White describe an audit of anaesthetic waste collected from six theatres in one teaching hospital in the United Kingdom and identify potential improvements in the management of such waste. Around 540 kg of solid anaesthetic waste was produced (about 2300 kg per theatre per year), 40% of which was potentially recyclable paper, card, plastic, and glass. Analysis of five sharps bins found that only 4% by weight was true sharps waste (needles and broken glass)—57% was glass and 39% was “other” (packaging, plastic, metal, and fluid).

Last year’s World Health Assembly adopted a powerful resolution on climate change, which not only warned of the stark consequences for human health but also identified how the health sector should respond to the profound changes taking place in the global ecosystem. The direct contribution of the health sector to environmental degradation is however less well analysed and debated. It is clear that the scale of carbon reduction needed to limit the effects of global warming cannot be achieved without the health sector playing its part.

Analysis of the carbon footprint of the NHS in England gave surprising results. About 18% of the NHS carbon footprint came from staff and patient travel, 22% from energy usage, and 59% from procurement. The management of such waste.

Clearly a detailed cost-benefit analysis is warranted.

Managing research data for future use

The BMJ is now asking authors for data sharing statements

For some time the BMJ has been watching other journals’ efforts to encourage authors to make raw research data available. Now we are taking part too, by asking authors to include a data sharing statement at the end of each original research article. The statement will explain which additional data—if any—are available, to whom, and how. Those data could range from additional explanatory material to the complete dataset. People allowed access to the data might range from fellow researchers to everyone. And data might be available only on request, accessible online with a password, or openly accessible to all on the web with a link on bmj.com.

We understand that many authors wish to guard data until they have published all their own papers, and we know that data sharing is hard to do. But we hope that authors will, increasingly, set the data free, perhaps after a set period of personal use.

Data sharing means more than the open access publication of articles and the posting in online registries of raw data as part of patient recruitment procedures.
study protocols and main results. Sharing allows other researchers—and perhaps scientists, clinicians, and patients—access to raw numbers, analyses, facts, ideas, and images that do not make it into published articles and registries. At its fullest extent, data sharing means free access for everyone. Many people would call this a moral obligation because most research is publicly funded and involves the public as participants. Other potential benefits include quicker scientific discovery and learning, better understanding of research methods and results, more transparency about the quality of research, and greater ability to confirm or refute research through replication.

Such sharing raises important questions about who owns the data,1 who gives permission to release the data (including funders, research participants, owners of the intellectual property, and copyright holders), where and how the data should be stored (in electronic repositories managed locally, nationally, or internationally; or in subject specific databases), how the data should be stored and managed and made compatible across repositories, how the data should be accessed and mined, who should have access and when, and what limits may be needed to prevent misuse and mishandling of data. Yet, despite these and other complexities, the movement to free the world’s vast swatches of untapped research data is gathering speed.

This momentum is coming not just from a few open access advocates and proponents of making the web a searchable network of data as well as articles.2 As delegates at the UK Research Data Service (UKRDS) conference in London heard last month, many researchers would also like access to unpublished raw data.3 Yet academic, technology, publishing, and business interests currently conspire—deliberately or not—to keep data hidden away. Researchers lack the incentives and the means to analyse all the data that they generate, to manage data after funded projects have ended, and to share data other than informally with certain collaborators. A recent UKRDS study on the logistics and costs of developing and maintaining a national shared digital research data service concluded that such a service is feasible and worth funding, and that it could greatly increase UK universities’ potential for research and innovation and their global competitiveness.4 Meanwhile, many other countries are already on the case.

Data sharing is hardly a new idea. Physicists, environmentalists, and researchers in the basic biomedical sciences have been doing this for years. Funders such as the UK Medical Research Council,5 US National Institutes of Health,6 and Wellcome Trust7 already mandate sharing of data from research in basic science and genetics. The US National Heart, Lung, and Blood Institute has opened up to researchers worldwide its collection of genetic and clinical data from three asthma research networks and the Framingham Heart Study.8 Even GlaxoSmithKline has opened up its “patent pool” so that data relevant to finding drugs for neglected diseases can be explored by other researchers.9

Numerous science journals mandate data sharing too. For example, a condition of publication in a Nature journal is that “authors are required to make materials, data and associated protocols promptly available to others without preconditions. Data sets must be made freely available to readers from the date of publication, and must be provided to editors and peer-reviewers at submission, for the purposes of evaluating the manuscript. For the following types of data set, submission to a community-endorsed, public repository is mandatory.”10 These data sets include those containing DNA and protein sequences, macromolecular structures, microarray data, and chemical compound screening.

For most medical journals, however, sharing of clinical research data is a new and difficult concept. Last week the editors of the open access BioMed Central journal Trials spelled out the main ethical and editorial barriers to data sharing in medicine and, partly drawing on discussions with scientists and other editors (including TG), proposed some solutions (box).11 The maintenance of patient confidentiality is a major challenge, because the combination of clinical data and personal data and the place of research can be enough to reveal a research participant’s identity. Hence clinical research data need to be anonymised carefully before sharing and, if a risk of identification remains, patients should be asked for consent to data sharing as well as consent to taking part in the research.

Since 2007, the Annals of Internal Medicine has been asking authors to make a “reproducible research statement” at the end of each research paper.12 Authors state whether and within what limits they will share the original study protocol, the dataset used for the analysis, and the computer code used to produce the results. We gladly acknowledge that we are emulating this policy in introducing data sharing statements for BMJ research articles and bringing data sharing to authors’ and readers’ attention. We hope authors and readers will now join us in this debate and will help journals to set data free.

5 Medical Research Council. MRC policy on data sharing and preservation. 2009. www.mrc.ac.uk/OurResearch/EthicsResearchGuidance/DatasharingInitiative/Policy/
MRC002551.