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Deciding who to admit to a critical care unit

Scarce resources may cause doctors to be pessimistic about prognosis and refuse critical care admissions

Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality worldwide. The incidence of COPD is rising, and the World Health Organization estimates that it will be the fourth leading cause of death globally by 2030. In this week’s BMJ, Wildman and colleagues report the differences between actual survival and survival predicted by a doctor in people with asthma or COPD admitted to intensive care. This is an important matter to investigate, because people with asthma and COPD who have acute exacerbations that require admission to intensive care have high short term mortality.1

Using data from 832 admissions for asthma or COPD in 95 intensive care units and high dependency units in the United Kingdom, the authors found that predicted survival was lower than actual survival (49% v 62%) 180 days after admission. This “prognostic pessimism” was present in the overall sample and for most subgroups of people. The absolute difference between predicted and actual survival was >30% in people with the lowest predicted survival. The authors suggest that the scarcity of intensive care resources in the UK may contribute to doctors’ inaccurate predictions of survival because such prognostic pessimism may stop them feeling that they are denying treatable patients potentially life saving treatment. Is such prognostic pessimism a disease that needs treatment (by improving doctors’ prognostic skills) or a symptom of an underlying problem with the healthcare system, such as scarce intensive care resources?

Decisions about the use of life sustaining treatment are complex, imprecise, and need to balance the potential risks and benefits to each critically ill person. Predicting the probability of short term survival is important when assessing the benefits of intensive care. Despite knowledge of important prognostic factors, previous studies have also shown significant variability in doctors’ estimates of survival for people with an exacerbation of COPD who need mechanical ventilation.3 4

Mortality should not be the only consideration when deciding about admission to intensive care. Providing doctors, patients, and families with more accurate estimates of survival during serious illness did not strongly influence the medical decisions made in a large study from the United States.5 Quality of life after intensive care is an important consideration also, especially as—for instance—nearly 90% of seriously ill people would rather die than survive with severe cognitive impairment.6 These factors may have had an effect on doctors’ predicted prognosis, but this cannot be determined on the basis of data provided in Wildman and colleagues’ study.7 Like predicting patient mortality, the ability of doctors and nurses to predict quality of life after intensive care is unsatisfactory.8

Making decisions about admission to intensive care is even more complex than determining the benefits and risks to an individual patient when resources are scarce. This may be especially relevant in the UK and southern Europe, where intensive care beds are often lacking.9 The authors speculate that in the face of chronically scarce resources, doctors may develop prognostic pessimism, which leads them to refuse seriously ill patients admission to intensive care. A study comparing admission to intensive care in Canada and the US reported that Alberta had 50% fewer intensive care beds per capita than did western Massachusetts. In the Canadian setting, admission to intensive care was more often denied to elderly patients with chronic medical conditions who were thought unlikely to benefit from such care.10 Although this illustrates rationing of intensive care on the basis of the availability of resource in Canada, it is unclear whether prognostic pessimism was a factor in the decision making process. Furthermore, the study found no significant difference in hospital mortality despite rationing of intensive care—hospital mortality was not reported in the study by Wildman and colleagues.2

Future studies of doctors’ prognostic accuracy in jurisdictions with fewer limitations in intensive care resources may allow Wildman and colleagues’ work to be interpreted within a broader context. This will determine whether prognostic pessimism requires intervention aimed at doctors or at underlying healthcare systems that have inadequate provision of critical care services.

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Competing interests: RS and MG are co-chairs of the Climate and Health Council. FG is vice chair of the Climate and Health Council. RH is a member of the council.
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Doctors and climate change

Health professionals have a duty to be part of the solution

One of the two duties of a doctor laid down by the General Medical Council of the United Kingdom is “to protect and promote the health of . . . the public.” Should this duty extend to working to prevent climate change? We believe it should.

Climate change leads to the extinction of species. During the past 500 million years—a mere 10th of the world’s history—five major and many minor events have caused extinctions. The last major event eliminated the dinosaurs 65 million years ago. An extraterrestrial object 10 km in diameter slammed into what is now the Yucatan peninsula, Mexico. It caused firestorms, a tsunami 1 km high, planet wide darkness for months, and an extended period of carbon dioxide induced global warming. Within a few months of the event, the 150 million year reign of the dinosaurs was over, and the space for mammalian evolution was created. The present climate related extinction event, so far a minor one, is caused by humans. Excessive amounts of carbon dioxide are being poured into the atmosphere as a result of human activity, even though we know what the consequences will be. These consequences are starkly spelt out in the latest Intergovernmental Panel on Climate Change and Stern reports.

Alterations in food production, with expected decreases in areas already under stress; rises in sea levels; the spread of vector borne disease; and water shortages are already aggravating health problems, particularly in poor countries. The impact of climate change will get much worse, and predictions of a hundred million climate refugees is no longer fanciful.

Health professionals must show leadership in tackling the potentially catastrophic effects of climate change. The Climate and Health Council was set up at the instigation of concerned doctors, and it has evolved over the past year into a focus for international action. Membership of the council is open to individuals and organisations. Many people have already signed the declaration (www.climateandhealth.org), and readers are invited to add their signatures.

The council sets out four ways in which health professionals should act. Firstly, we should inform our professional colleagues and the wider community about the health consequences of climate change, and the major health benefits that will result from tackling it, including a reduction in the prevalence of obesity in rich countries. Secondly, we should set an example by reducing our personal carbon footprints and ensuring that the organisations we work for do likewise. Thirdly, we should advocate. The international community recognises that a post Kyoto global framework is an essential part of any solution. Our advocacy must insist that this framework promotes health. To this end, the framework must constrain carbon dioxide emissions so that atmospheric levels do not exceed 450 parts per million, the level at which the odds for avoiding dangerous climate change are better than 50:50. The framework must also be the basis for ensuring a transfer of resources to give time to those countries

that are undergoing, or have yet to undergo, the social and economic transition that fossil fuel has enabled in the rich Western world. The framework based market of contraction and convergence achieves both these aims, and is the most feasible option at present.\textsuperscript{10} Health professionals should make a concerted effort to contribute to the post Kyoto framework, and to lobby at the United Nations’ conferences on climate change in Bali in December and then in Copenhagen in November 2009.

Fourthly, health professionals should seek innovative approaches to using our many networks, such as specialty associations, to facilitate the necessary changes to recruit as many organisations, institutions, and individuals as possible.

Climate change challenges the health of everybody, but particularly of people with the fewest resources. It is the major challenge of the 21st century. Unless we cap carbon emissions in ways that ensure transfer of resources to the poorer nations, we may all go the way of the dinosaurs, and the going will not be comfortable. The Climate and Health Council will be as strong as its collective membership. By adding your voice to the council and taking the necessary actions, you can help to ensure that health professionals are, in the best of our traditions, part of the solution.

3 HM Treasury. Stern review final report. 2006. www.hm-treasury.gov.uk/independent_reviews/stern_review_economics_climate_change/sternreview_index.cfm.

**Screening for prostate cancer in younger men**

Clinicians should promote informed decision making while awaiting definitive evidence from RCTs

Current policies on screening for prostate cancer vary worldwide. This discrepancy can be explained in part by the lack of clear evidence to support or refute such screening. Evidence is lacking for the diagnostic accuracy of current screening tests (digital rectal examination and prostate specific antigen testing) and whether screening ultimately improves survival and quality of life.\textsuperscript{1} In their study in this week’s BMJ, Lane and colleagues present results from the prostate testing for cancer and treatment study, which assesses the feasibility of testing for prostate cancer in younger men (45-49 years).\textsuperscript{2}

A recent systematic review\textsuperscript{3} identified two randomised controlled trials (RCTs) assessing the effectiveness of screening for prostate cancer.\textsuperscript{4} Both trials had several methodological weaknesses. Reanalysis of these trials using an intention to treat analysis showed no significant reduction in mortality between men randomised to screening and men in control groups (relative risk 1.01, 95% confidence interval 0.76 to 1.33). The review concluded that these trials found insufficient evidence to support or refute screening for prostate cancer.

In the presence of such uncertainty further evidence from methodologically robust studies is needed to determine the effect of screening for prostate cancer on prostate cancer specific mortality, quality of life, potential harms, and costs. The results of several ongoing trials are awaited.\textsuperscript{5,7}

Lane and colleagues report the uptake of prostate specific antigen testing, the positive predictive value of prostate specific antigen, and the clinical features of detected cancers in 442 UK men aged 45-49, using a prostate specific antigen age based threshold for biopsy of 1.5 ng/ml. They show that this group of men will accept testing for prostate cancer, albeit at a much lower rate than older men. Using this reference range, Lane and colleagues diagnosed prostate cancer in 10 of the 442 men. Five of these cases were classified as potentially clinically relevant.

Although this paper makes an important contribution to our knowledge of age specific prostate specific antigen thresholds in a white population in the United Kingdom, the final decision regarding widespread screening should be based on reliable population based data, preferably from high quality RCTs. Such data will provide strong evidence on the effects of screening on individual patient outcomes. As Lane and colleagues point out, the results of their paper, and others on age specific prostate specific antigen thresholds, should be interpreted with caution until results from ongoing RCTs determining the effects of screening at a population level are available.

In the absence of evidence to guide clinicians about whether or not to screen men for prostate cancer, many governing medical bodies currently recommend informed discussion between patient and doctor when contemplating screening for prostate cancer. But can a patient be truly informed if medical professionals and researchers are still investigating what the best course of action is? In cases such as this, evidence based practitioners place greater emphasis on the clinician’s experience and the patient’s values to facilitate informed discussion and decision making.

**RESEARCH, p 1139**

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Competing interests: SG is senior lecturer, Andrology Australia, which is a community and professional education programme funded by the Australian government that provides health information on male reproductive health.

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**EDITORIALS**

**Screening for prostate cancer in younger men**

Clinicians should promote informed decision making while awaiting definitive evidence from RCTs.
Lack of knowledge, limited access to high quality educational materials, and psychosocial attitudes may all act as barriers for men when seeking and participating in discussion with clinicians about screening for prostate cancer. These factors may all increase conflict in making decisions or uncertainty associated with treatment. A systematic review of decision aids for people facing screening and treatment decisions found that decision aids increased consumer knowledge, lowered conflict when making decisions, and promoted greater agreement between patient values and the final decision.

Screening for prostate cancer is now commonplace in many settings, despite the lack of evidence from ongoing randomised controlled trials. The paper by Lane and colleagues provides useful information on the prevalence of prostate cancer and diagnostic accuracy of different screening tests. It is also beneficial to understand the acceptability of prostate cancer screening in younger men, because this adds to the growing body of literature on patient preference and may be useful when planning ways to promote the uptake of screening. However, as Lane and colleagues point out, such data will be most useful if the ongoing randomised controlled trials show that screening for prostate cancer is effective.

Clinicians and consumers currently stumble through the darkness that pervades the debate on screening for prostate cancer. Until the results of ongoing RCTs can shed light on this important clinical and policy decision, we recommend informed discussion between clinicians and patients about the benefits, potential harms, and limitations of screening. Greater uptake of patient education and decision aids, and incorporation of the clinician’s experience and expertise, may help overcome the barriers to discussion and facilitate an informed decision.


Communicating risk to the public after radiological incidents
Providing detailed, comprehensive, and relevant health information is essential

In this week’s BMJ, Rubin and colleagues report a cross sectional survey and qualitative analysis of perceptions of risk and strategies to communicate risk in relation to the poisoning of Alexander Litvinenko with polonium-210 in London in 2006. The study breaks new ground, not only because it examines an important public health incident in a major metropolitan area, but because it is one of the first studies of behaviour and risk communication after an incident involving the intentional release of radioactive materials. As such, it offers valuable insights into emergency preparedness.

Major incidents involving radioactive materials can pose many challenges for emergency services, hospitals, and health departments. These include identifying the presence, type, and extent of contamination; issuing guidance on protective actions; implementing decontamination procedures; arranging health screening for potentially affected people; providing necessary treatment (for example, for internal contamination); and organising long term follow-up of affected populations.

The extent of difficulty in meeting these challenges depends on several factors—one of the most important of which is public reaction. Risk research has shown that radiation is one of the most feared of all hazards, and situations involving radioactive contamination produce a great deal of apprehension, alarm, and dread. Furthermore, as research and historical experience have shown, people’s concerns have the potential to translate into behavioural responses that complicate the situation. 3-5 This is often true when information is confusing or in short supply. Such an example occurred during the 1979 Three Mile Island nuclear accident in the United States, when people received inadequate and conflicting information. Ultimately, for each person advised to evacuate, nearly 45 actually did. In all, nearly 150000 people fled the area. 6

Radiological incidents can also cause chronic stress in unexposed people and can lead to healthcare facilities being overwhelmed by worried people. After a caesium-137 incident tragically took four lives in Brazil in 1987, around 112000 people sought radiological monitoring in special facilities. Social stigma and discrimination against people and products from an affected area are also common after radiological incidents. These phenomena, which can complicate recovery efforts, were seen after the 1986 Chernobyl disaster and after incidents in Brazil in 1987, Japan in 1999, and Thailand in 2000.7 8

The above experience relates to accidents involving...
Obesity and cancer

Substantial evidence supports the link between increasing adiposity and a higher risk of many cancers

Obesity is an important cause of type 2 diabetes mellitus, hypertension, and dyslipidaemia. The adverse metabolic effects of excess body fat accelerate the development of atheroma and increase the risk of coronary heart disease, stroke, and early death. The association between adiposity and cancer, however, is less well known. In this week’s BMJ, Reeves and colleagues report a large prospective cohort study from the United Kingdom—the million women study—which assesses the association between body mass index (BMI) and cancer incidence and mortality.1

In 2002, the International Agency for Research on Cancer (IARC) convened an expert panel—which would draw on epidemiological, clinical, and experimental data—to evaluate the link between weight and cancer.2 It concluded that some colon cancers, postmenopausal breast cancers, endometrial cancers, kidney cancers, and adenocarcinomas of the oesophagus could be prevented by avoiding weight gain. Since the IARC report, many observational studies have investigated the association between adiposity and cancer. The results indicate that more cancers are probably linked to obesity than was thought originally, including adenocarcinoma of the gastric cardia, gallbladder cancer, liver cancer, pancreatic cancer, haematopoietic cancers, and advanced prostate cancer.3,4

Reeves and colleagues’ study evaluates the effect of BMI on the incidence of cancer and mortality from cancer in more than a million women aged 50-64. Increases in BMI on the incidence of cancer and mortality from cancer, liver cancer, kidney cancer, and colorectal cancer were strongly statistically significant.5

Increasing BMI was associated with significantly increased incidence of postmenopausal breast cancer, endometrial cancer, kidney cancer, and adenocarcinoma of...
the oesophagus, in agreement with the IARC review. Higher BMI was also significantly related to the risk of leukaemia, multiple myeloma, non-Hodgkin’s lymphoma, pancreatic cancer, and ovarian cancer.

These findings are generally in agreement with accumulated evidence to date. Most available studies of the relation between haematopoietic cancers and BMI—although smaller than the current study—have reported increases in the risk of non-Hodgkin’s lymphoma, multiple myeloma, and leukaemia. Relative risks from these studies have generally been between 1.2 and 2.0.

Recent studies also suggest that high BMI is associated with increased risk for pancreatic cancer, with relative risk estimates for obesity generally between 1.5 and 2.0. However, some studies have found smaller positive associations. Evidence indicates that the association between adiposity and pancreatic cancer is non-linear, and increased risk is not seen until BMI reaches 30. Chronic hyperinsulinaemia and glucose intolerance may contribute to an increased risk of pancreatic cancer. A recent study suggests that people with insulin resistance who are in the highest quarter of fasting concentrations of serum glucose and insulin have more than double the risk of pancreatic cancer than those in the lowest quarter. Another study found that a tendency towards central (versus peripheral) weight gain was associated with a 45% increase in risk of pancreatic cancer after adjustment for the independent effects of general adiposity. The variability in estimates of risk associated with BMI for pancreatic cancer may partly result from using BMI, rather than a measure of central adiposity, as the measure of exposure.

Reeves and colleagues’ study found no association between BMI and colorectal cancer in postmenopausal women—who comprised most of the women studied. Studies in different populations have consistently found that obesity is a stronger predictor of colorectal cancer in men than in women. The reasons for this sex difference are unclear. One hypothesis is that central adiposity, which occurs more often in men, is a stronger predictor of colon cancer risk than peripheral adiposity or general overweight. Recent prospective cohort studies examining the predictive value of various anthropometric measurements for the risk of colon cancer found that waist circumference was an independent risk factor for colon cancer that was stronger than BMI. This association was seen in both women and men. Thus, abdominal obesity is probably a more important predictor of colon cancer than general overweight; this might explain the differences in the findings of the UK study.

Substantial observational evidence suggests that increasing adiposity—both overall and central—is associated with increasing risk of many cancers. The strongest empirical support for mechanisms to link obesity and cancer risk involves the metabolic and endocrine effects of obesity, and the alterations they induce in the production of peptide and steroid hormones. The worldwide obesity epidemic shows no signs of abating, so insights into the mechanisms by which obesity contributes to the formation and progression of tumours is urgently needed, as are new approaches to intervene in this process.

There may be a treatment

Although the track record for successful treatment interventions for acute bronchiolitis has so far been unimpressive, 1 a recent trial using nebulised hypertonic saline holds promise. 2 This study involved 96 infants with a mean age of 4.7 months admitted to hospital for acute bronchiolitis, who were double blindly randomised to receive nebulised 3% saline or 0.9% saline. The infants in the hypertonic saline group had a clinically significant 26% reduction in length of hospital stay (2.6 vs 3.5 days). Treatment was well tolerated with no observed adverse side effects.

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Competing interests: None declared.


COMMUNITY ACQUIRED PNEUMONIA

Antibiotic coverage is atypical: evidence from randomised trials

Bjerre quotes an observational study to support the addition of antibiotics that cover atypical pathogens to the treatment of patients with community acquired pneumonia. 1 The results of randomised controlled trials dealing with this question were amassed in two recent systematic reviews and meta-analyses (one published in the BMJ) which were not quoted in the editorial. 2, 3 Our systematic review included 24 trials, which randomised 5015 patients. 3 Mortality was no different in the arm that provided atypical coverage and the arm that did not (relative risk 1.13, 95% confidence interval 0.82 to 1.54). Regimens that covered atypical pathogens showed a trend towards clinical success and a significant advantage to bacteriological eradication. Both disappeared when evaluating methodologically high quality studies alone. Nearly all studies compared a β lactam with a single quinolone or macrolide. A randomised clinical trial comparing treatment with a β lactam to a combination of a β lactam and a macrolide is needed.

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Competing interests: None declared.

1 Bjerre LM. Management of community acquired pneumonia. BMJ 2007;335:1004-5. (17 November.)
colectomy is not “strong evidence suggesting that the threshold for elective colectomy is too high.” Patients who electively undergo colectomy usually have chronic relapsing disease or risk of malignancy, whereas those admitted to hospital for medical management or emergency colectomy are usually far sicker with severe acute or fulminant disease. These subgroups of patients have entirely different indications for colectomy, so lowering the threshold for elective surgery would not necessarily reduce numbers being admitted with severe acute disease.

Secondly, the authors’ method of risk adjustment for comorbidity is flawed given the poor accuracy and completeness of secondary medical diagnostic coding in the hospital episode statistics database. Furthermore, their risk model did not include well established predictors of the need for colectomy, such as extent of IBD and race, or take the severity of comorbid disease into account. It therefore assumed that patients with mild and severe comorbid disease have the same risk of mortality. Patients treated medically may have been high risk surgical candidates with poor prognosis who were appropriately not offered surgery. This contention is supported by the authors’ observation that patients managed conservatively during their index hospital admission had high mortality irrespective of whether they subsequently underwent colectomy.

No evidence exists to change the current practice of consigning surgery in IBD to the treatment of last resort.

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Competing interests: None declared.


FOREIGN DOCTORS’ VICTORY

British benevolence and betrayal

As a qualified clinical epidemiologist, I had an excellent position abroad but migrated to the UK in 2002 under the highly skilled migrant programme (HSMP) because of various ties with the UK. I declared the UK my main home and invested my life savings in the country. I was welcomed with open arms by NHS colleagues. When my application was approved, government documents and communications led me to believe that I could apply for indefinite leave to remain (ILR) after four years.

When the first highly skilled migrants were close to applying for ILR, the government retrospectively lengthened the qualifying period to five years. I had to pay an extra £15,000 (£20900; £31000) in university fees for three years. Fees for many applications to the Home Office increased steeply. Travel continued to be expensive and difficult as visas were needed for mainland Europe.

A joint parliamentary committee concluded that these changes were “not compatible with the right to respect for home and family life under Article 8 ECHR and contrary to basic notions of fairness.” It recommended that the changes should apply prospectively, and that those already granted leave to remain under HSMP should be treated according to the previous rules.

On behalf of thousands of highly skilled migrants who have made the UK their home and who perform their civic duties, I appeal to the UK government to be fair and not to cause enormous misery and hardship by changing the rules of the game midway.

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Competing interests: I have been both personally and financially severely disadvantaged due to the changes introduced midway through the scheme while I was on the HSMP visa.
1. Dyer C. Foreign doctors win High Court challenge over training places. BMJ 2007;335:1009. (17 November.)

CLIMATE CHANGE AND HEALTH

We must all act now

See also Editorial by Stott et al and News by Watson

Almost everyone agrees that human production of greenhouse gases is driving global warming—more quickly than anticipated.1 The latest summary of the scientific evidence by the Intergovernmental Panel on Climate Change (IPCC) suggests that by 2030 the earth will warm by 2.0°C—the tipping point at which warming may lead to more warming.2 Temperatures may rise by 6.4°C this century.

In Bali next week, world leaders will try to agree how to limit this rise. It is imperative that they do. The IPCC predicts increased death and injury due to heatwaves, floods, storms, fires, and droughts. Cardiorespiratory disease will increase because of higher ozone concentrations. Freshwater and saltwater flooding will increase the spread of diarrhoea.3 By 2100, the number of people exposed to malaria prone temperatures may increase by a third. Water availability will suffer. Subsistence agriculture will fail through changes to the climate and ecosystem collapse. Hunger, migration, and war may also be driven by economic collapse similar in scale to that associated with world wars.4

As doctors we urge the leaders to consider the health implications of climate change and act now to prevent it. The most vulnerable people will be affected first. Around 175 million children are predicted to be afflicted each year over the next decade by disasters caused by climate change; by 2010, 50 million people may be displaced, mostly women and children.5

We consider this to be the greatest public health disaster facing us today and one that requires action at all levels. We call on all health professionals to urge their colleagues, employers, and institutions to reduce their carbon footprint and to set an example in their personal lives. We intend to make our colleges carbon neutral as soon as possible. Above all, we call on the world’s leaders to take radical action to reduce CO2 emissions as a matter of extreme urgency. Only by firm and decisive action now, can we, as a global community, hope to avert or mitigate an impending public health catastrophe of immense proportions.

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Competing interests: None declared.

Drug companies are ignoring health crisis in poor countries

Adrian O’Dowd

The drug industry is “burying its head in the sand” when dealing with health in developing countries and denying poorer people access to life-saving drugs, a report claims this week.

A critical report by the international agency Oxfam says that the drug industry is refusing to change the way it does business in poor countries, despite promising that it would, and is undermining its own future.

Oxfam’s report looks at the world’s top 12 drug companies, including their drug pricing policies, their record in developing drugs that are relevant to health care in poor countries, and their stance on protecting intellectual property rights.

The report says that the industry shows various shortcomings, including:

• Failure to implement a systematic and transparent tiered pricing policy that is based on people’s ability to pay
• Continuing to neglect research and development concerning diseases that affect developing countries, and
• Inflexibility in protecting intellectual property, which includes challenging poor countries in court to stop them using legal safeguards to protect public health.

Oxfam interviewed 12 companies in preparing the report: Abbott, AstraZeneca, Bristol-Myers Squibb, GlaxoSmithKline, Eli Lilly, Johnson & Johnson, Merck, Novartis, Pfizer, Roche, Sanofi-Aventis, and Wyeth.

In 2002 Oxfam, Save the Children, and Voluntary Service Overseas published Beyond Philanthropy, a report calling for the drug industry to contribute to solving the health crisis in developing countries. The new Oxfam report assesses what has changed since then and says that the industry has made only “halting progress” in some areas.

Oxfam’s head of research, Sumi Dhanarajan, said, “The industry is operating in a shortsighted way, because it could gain enormous benefits from emerging markets … The industry is burying its head in the sand.”

Investing for Life is available at www.oxfam.org.uk.

UN is attacked for “catatonic passivity” by former envoy

Zosia Kmietowicz LONDON

The former United Nations special envoy for AIDS in Africa has issued a scathing condemnation of UNAIDS (the joint UN and World Health Organization programme on HIV and AIDS) for its “catatonic passivity” in the face of the epidemic. He has also delivered a blistering criticism of the agency’s latest report on prevalence.

Stephen Lewis (above), who worked for the UN for more than two decades, holding the post of special envoy between 2001 and 2006, attacked UNAIDS for “delaying and dithering” in producing revised figures on the prevalence of HIV and AIDS. He said the resulting report, the 2007 AIDS Epidemic Update, had served to divert the world’s attention away from the “continuing apocalypse for sub-Saharan Africa” by focusing instead on the mathematical models and reasons for the adjusted figures.

The report, which was released last week (bmj.com, 24 Nov, News Extra), showed that UNAIDS had overestimated the scale of the epidemic in 2007 and that the number of people with HIV or AIDS was 33 million rather than the 40 million it had previously given.

UNAIDS was “stubborn and sloppy” in the way it had compiled the figures, said Mr Lewis, who is currently codirector of the campaigning group AIDS-Free World and professor of global health at McMaster University, Hamilton, Ontario. For many years it had ignored calls from “knowledgeable epidemiologists” to revise the prevalence estimates, he said.

“It doesn’t take a Nobel prize statistician to guess that prevalence rates based on urban antenatal clinics should not be extrapolated to the entire country and presented as holy writ,” Mr Lewis said at a briefing in London ahead of world AIDS day on 1 December.

The slow response had undermined public confidence in the figures and led to “unnecessary levels of doubt, contention, and confusion,” he said.

Mr Lewis accused UNAIDS and its 10 cosponsors, which include Unicef, WHO, and the World Bank, of passivity in the face of the HIV and AIDS epidemic.

“More than 25 years into the pandemic we have an epidemic update that is horrifying in its implications. Whether it’s 40 million or 33 million, this plague continues to ravage humankind. I simply do not believe that the UN has done everything it can possibly do to turn the tide. And I don’t mean the member states, I mean the secretariat,” he said.

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NEWS
More than four in 10 women were not offered the choice of a home birth, report says

Zosia Kmietowicz LONDON

Pregnant women in England are not being offered the choice and care laid down in national guidelines, a survey of new mothers shows.

The survey, which was carried out by the Healthcare Commission, showed that women are generally fairly happy with maternity services. Overall the percentage of women who said that their care was excellent, very good, or good was 89% during pregnancy, 90% during labour and birth, and 80% after the birth.

But the commission said that in some areas the feedback from women was less positive and that there was wide variability in satisfaction between trusts.

More than four in 10 women were not offered the choice to have their baby at home, as recommended in guidelines from the National Institute for Health and Clinical Excellence (NICE). But while the percentage who were not given this option was as low as 8% in some trusts, in others it was 76%.

A similar proportion of women (36%) were not offered NHS antenatal classes, which the government said trusts should do in its national framework for children, young people, and maternity services. But again in some trusts this figure was 76%.

The survey, which was carried out in trusts in England and completed by 26000 women who gave birth in January and February this year, also found that more than a quarter of women (26%) were left alone during labour or shortly after giving birth at a time that worried them. And more than half (57%) said that they had been lying down when giving birth or that stirrups had been used—practices that are discouraged in NICE guidelines.

Most women said they were treated with kindness and understanding, although at one trust 18% of respondents said this was not their experience.

In terms of aftercare more than 30% of women looked after in 21 trusts (of a total of 148) said they did not get enough food. Overall 22% of women said they would have liked to have seen a midwife more often after birth, and 19% said that the toilets and bathrooms at the hospital were “not very clean” or “not clean at all.”

Anna Walker, chief executive of the commission, said, “Overall, women are clearly positive about maternity services. But the results do highlight specific areas of concern and wide variations with issues, including postnatal care, communication, food, and cleanliness.

“These results show us that many trusts provide very positive services for women. Trusts with less positive results need to learn from the good performers.”

The commission is due to publish detailed results of its comprehensive review early next year.

Women’s Experiences of Maternity Services in the NHS in England is at www.healthcarecommission.org.uk

Reprogramming of skin cells to create embryonic stem cells

Geoff Watts LONDON

Last week’s announcement that human embryonic stem cells have been successfully created by reprogramming skin cells (making them behave like embryonic stem cells) was welcomed by those scientists and others who had harboured ethical doubts about an enterprise that had previously depended on embryos.

But although stem cell scientists share this enthusiasm, they go on to point out that the new technique, in its current form, is potentially hazardous. This issue will have to be dealt with before reprogramming can be applied in clinical medicine.

At present the principal source of human embryonic stem cells is the pool of early embryos that are surplus to the requirements of women undergoing in vitro fertilisation.

Reprogramming dispenses with the need for embryonic material. It relies instead on making ordinary body cells return to an earlier developmental stage in which they regain the potentiality to give rise to any of the body’s 200 or more different cell types. Two research groups, one American and one Japanese, have achieved this aim.

Proof that the technique is feasible came last year when Shinya Yamanaka of Kyoto University reported the successful reprogramming of mouse skin cells. His is one of the two research groups that have now repeated the same feat with human cells, using a broadly similar technique.

The second group was based in the laboratory of James Thomson, a developmental biologist at the University of Wisconsin-Madison. Biologists have long believed that it should be possible to make any cell behave like an embryonic stem cell. The trick, it seems, is to add four genes to a somatic cell’s existing complement of DNA. When switched on, these genes code for a set of proteins that prompt the cell to exhibit embryonic properties. Two of the selected genes were used by both research groups; the other two were different.

Both groups also used viruses to insert the new genes into the
One in 20 East German doctors spied on patients or colleagues for the Stasi

Annette Tuffs HEIDELBERG
About 5% of doctors in the former East Germany spied on their colleagues or patients as unofficial members of the East German secret police (the Staatssicherheit or Stasi), a new report has shown.

The study, by the Hannah Arendt Institute for Research on Totalitarianism, Dresden, and commissioned by the German Medical Association and the German medical journal Deutsches Ärzteblatt, showed that the percentage of unofficial members of the Stasi among doctors was higher than in the East German population as a whole.

“Doctors were one of the main targets of the Stasi because they were thought to belong to a reactionary class and were thought to be especially interested in escaping to West Germany,” said Francesca Weil, author of the study, at a press conference last week in Berlin.

The study looked at a representative sample of doctors who worked in East Germany and at 493 files in the central Stasi archive. Twenty one of the doctors who had acted as unofficial spies agreed to be interviewed.

Of those doctors who were unofficial spies, about a quarter passed on information not only about colleagues but also about their patients’ health and private lives. Psychiatrists and sports medicine experts were the most common specialists among the unofficial spies, and a third of them held a leading position in a hospital.

Reasons for spying varied. Some doctors were trying to advance their career or were afraid that their careers would suffer if they did not participate; others were committed socialists; and another group liked the economic advantages. Zielgruppe Ärzteschaft is available at www.hait.tu-dresden.de/ext/details.asp?reihe=2&nr=152.

Diabetes expert accuses drug company of “intimidation”

Bob Burton CANBERRA
The former chairman of research and development at GlaxoSmithKline (GSK), Tadataka Yamada, has been asked by a US Senate committee to explain his role in what it describes as the “intimidation” of John Buse, a professor of medicine at the University of North Carolina.

In 1999 Dr Buse raised questions about the cardiovascular safety of the diabetes drug rosiglitazone, which is marketed as Avandia (BMJ 2007;334:1237). He was speaking at a symposium organised by the American Diabetes Association.

A report by the Senate Finance Committee staff has shown that a company official emailed Dr Yamada proposing that a “firm letter” be written to Dr Buse containing a warning that “the punishment will be that we will complain up his academic line and to the CME [continuing medical education] granting bodies that accredit his activities.”

In response Dr Yamada wrote: “I think there are two courses of action. One is to sue him for knowingly defaming our product even after we have set him straight as to the facts—the other is to launch a well planned offensive on behalf of Avandia.”

The report also says that Dr Yamada telephoned the chairman of Dr Buse’s department, Fred Sparling.

In a media statement issued after the release of the report the company defended its actions but conceded that “perhaps we could have handled interactions with Dr Buse better.”

Tabling the report, the Republican senator Charles Grassley, of Iowa, expressed concern that the case may indicate a wider problem. “Not even I was aware of the scope of the attention that I had garnered at SKB [as GSK then was]. I am concerned that Senator Grassley may be correct.”

Dr Yamada was unavailable for comment.

The US Food and Drug Administration has recently upgraded the “black box” warning for rosiglitazone.

IN BRIEF

US health costs face major increase: The Congressional Budget Office said that federal spending on the Medicare health insurance programme for elderly people and on Medicaid for poor people will rise, within 75 years, to 19% of the gross domestic product (GDP) from the current 4%. Total US spending on health care will rise from the current 16% of GDP to 49%. The problem is not an ageing population, the office said, but greater health costs per person.

Israeli doctors back bill that would postpone treatment for violent patients: A parliamentary bill backed by the Israel Medical Association would allow Israeli hospitals to refuse medical treatment for up to six months to patients who have attacked medical staff. Three quarters of emergency room staff have witnessed physical or verbal violence in the past year.

Hospital food and cleanliness are improving in England: The latest figures from the National Patient Safety Agency show that 99.5% of hospitals in England were rated as “acceptable” or better for the food they provide and 98% were similarly rated for their patient environment, which includes cleanliness. The results show a steady improvement over the last three years.

Rift Valley fever spreads in Sudan: Cases in humans of Rift Valley fever continue to occur in Sudan, with more than 221 cases reported in the past two weeks. By 21 November a total of 436 cases of the disease, including 161 deaths, have been reported from White Nile, Sennar, and Gazeera states.

New body approves 40 UK trials units: Forty clinical trials units in the UK have been approved for registration with the new UK Clinical Research Collaboration (for a list see www.ukcrn.org.uk). To be registered, units have to show they have the expertise to conduct trials in line with appropriate standards and regulations or that they are working towards these.

UK steps up measures against flu pandemic: The UK government has increased its flu treatment and protection strategies in a new plan to increase preparedness against a possible pandemic. The new measures include doubling the stock of antivirals to cover at least 50% of the population and buying 14.7 million courses of antibiotics to cover people at risk. The national framework is available at www.dh.gov.uk.

Targeted screening for glaucoma may be cost effective

Susan Mayor LONDON

Targeted screening of particular groups for open angle glaucoma would be more cost effective than testing the general population, a UK modelling study concludes.

The study compared different strategies for screening for open angle glaucoma (the commonest type of glaucoma, which is the leading cause of irreversible blindness) by reviewing the existing research evidence for effectiveness and cost effectiveness.

One strategy was for a glaucoma screening technician to measure intraocular pressure and then do a second test from a range of possible tests to screen people considered to be at risk of open angle glaucoma. The United Kingdom doesn’t currently have glaucoma screening technicians, but the researchers assumed that staff could be trained and accredited in a similar way to retinal screening technicians who screen for diabetic retinopathy.

A second potential strategy—which costs more—involves patients at high risk being invited to be assessed by a glaucoma optometrist.

Positive results of screening in either strategy would result in the patient being referred for diagnosis by an ophthalmologist, as occurs currently.

Constraints on use of patients’ data are

Clare Dyer BMJ

Bodies that oversee medical research are harming public health by imposing constraints on the use of patients’ data that go further than the law demands, doctors were told at a meeting last week organised by the cardiothoracic section of the Royal Society of Medicine.

Charles Warlow, professor of medical neurology at Edinburgh University, quoted David Smith, deputy information commissioner at the UK Information Commissioner’s Office, as saying that the Data Protection Act did not necessarily require consent for the use of health information in medical research. Mr Smith had also approved comments by the medical law expert Philip Havers QC that “researchers should be bolder,” Professor Warlow said.

Mr Havers had said at a symposium in 2006: “The courts are likely to be highly receptive to arguments that the law justifies breaches of confidence and privacy with regard to secondary data research, provided [that] the infringements are no more than is necessary.”

The success of such arguments, Mr Havers added, would depend on demonstrating the strength of the public interest in using the data and “that it was simply not practicable to obtain the consent of the patient or to provide the patient with information about the research.”

Yet guidance from the General Medical Council and the NHS on confidentiality was much more stringent, Professor Warlow told participants at the meeting, which was entitled “The doctor under fire.”

Excluding people from research who did not consent introduced consent bias, he said. The Scottish intracranial malformation study was one opportunity to study the effects of
Less than half of men invited for screening for bowel cancer take up the offer, project shows

Roger Dobson ABERGAVENNY
A pilot project to test the acceptability of screening people for bowel cancer has shown a low uptake, with less than half of the men who were invited to take part doing so.

Uptake was also low in deprived areas and in some ethnic groups, says the report on the second round of the UK colorectal cancer screening pilot (British Journal of Cancer doi: 10.1038/sj.bjc.6604089).

The first round of the pilot took place in 2000-3 in two sites, one in England and one in Scotland (BMJ 2004;329:132-133). Of those who were invited to take part in the second round 84% had taken part in the first.

The report also warns that screening will significantly increase the need for services, especially endoscopy.

The bowel cancer screening programme is being rolled out across the United Kingdom and is expected to be fully in place by 2009. The aim of the pilot scheme was to assess the feasibility of introducing screening that is based on faecal occult blood testing.

The authors of the new report, from Edinburgh University, the Institute of Cancer Research, Sutton, and other centres, looked at the second round of the pilot, which took place only at the English site.

A total of 127 746 men and women aged 50-69 years were invited to participate, of whom 66 264 (52%) returned an adequate test kit. Uptake in the first round was 59%. A total of 1171 people had a positive test result, of whom 970 attended for colonoscopy.

Uptake in men (48% of those invited) was lower than in women (56%) (adjusted odds ratio 1.42 (95% confidence interval 1.36 to 1.48)). Uptake, however, increased with age, from 46% in men and women aged under 55 to 59% in those aged 65-9.

Uptake also fell as level of deprivation increased, from 61% among participants in the wealthiest areas to 37% among those in the poorest, and was also lower in areas with a high proportion of people of Indian subcontinental origin.

harming research

such bias, he added. These researchers were not able to get consent from all patients but had approval from the multicentre research ethics committee to collect baseline and follow-up data on the whole cohort from GPs’ and hospital records. The study showed that consenters were systematically different from those who hadn’t consented.

Richard Smith, a former editor of the BMJ, called for better protection for doctors who blow the whistle on research misconduct. Dr Smith said he had reported researchers for misconduct possibly 20 times a year when he was an editor. “Often my experience was miserable,” he said.

In one case he had rung the district general hospital that employed the doctor, to be told that he was already suspended for clinical reasons and that the hospital would investigate the BMJ’s complaint if the journal paid for it.

EU residents may be able to travel to any member state for care

Deborah Cohen BMJ
European Union residents will be able to travel to any of the 27 member states for non-emergency health care if new European Commission proposals are adopted.

A draft copy of the proposals seen by the BMJ attempts to set down legislation on patient mobility after the European Court of Justice ruled that health care should be part of a European free market.

Under the plans, which are expected to be published next week, patients should be able to receive health care similar to what they would be entitled to in their home country, with the costs covered up to “at least” the price of the similar care in their own country. However, member states will have to decide what the cost of treatment entails and whether, for example, it would include accommodation, food, and travel.

Although the proposals do not supersede earlier regulations—which allow local health authorities to sanction and pay for patients to travel abroad for prearranged treatment—the proposals say that anyone living in the EU should be able to travel to another member state for health care, whatever the reason, if it is deemed clinically appropriate.

Member states will still, however, be able to impose certain conditions identical to those that apply at the local level, such as the requirement to see a GP before a specialist.

Although the plans say that patients should not be given drugs or treatments that their own state system does not fund, sources within the Department of Health in England are worried that patients will use the directive to challenge availability of different treatments across the country.

A third of people in UK with HIV don’t know they are infected

Andrew Cole LONDON
Around a third of the estimated 73 000 adults in the United Kingdom who now have HIV remain unaware of their infection, despite a big increase in the number of people being tested, the latest figures from the Health Protection Agency indicate.

The agency’s annual report on HIV and other sexually transmitted diseases shows that the number of new infections of HIV fell a little last year, from 7 900 in 2005 to an estimated 7 800. But the incidence among gay men continues to rise, with 2 700 new cases reported in 2006—nearly two thirds of all HIV infections thought to have been acquired in the UK.

The incidence of other sexual infections among gay men has also risen sharply in the last five years, especially syphilis (up by 117%), chlamydia (97%), gonorrhoea (25%), non-specific urethritis (24%), and genital warts (21%).

Almost half of all new diagnoses of HIV in the UK were among black Africans, many of whom are thought to have contracted the disease outside the country, and 3.2% were among black Caribbeans. The percentage of people infected with HIV is much higher in these groups than in the white population: an estimated 4% of black Africans and 0.3% of black Caribbeans are infected, whereas the percentage of white people infected is 0.08%.

The latest figures also show a sharp fall in the number of deaths from the disease, from 749 in 1997 to 497 last year, with the biggest decrease in mortality occurring in the oldest age groups.

The report notes that more people than ever before are being tested for HIV and other sexually transmitted diseases and that waiting times to be seen at genitourinary clinics have shortened significantly. Despite this it estimates that a quarter of heterosexual people infected with HIV and almost half of gay men with it leave clinics unaware they are infected, having visited for other reasons or declined the test.

The government’s Independent Advisory Group on Sexual Health and HIV is calling on GPs to improve their contraceptive services as well as increasing screening for HIV.

Testing Times: HIV and Other Sexually Transmitted Infections in the United Kingdom, 2007 is available at www.hpa.org.uk.

Research into causes of disease needs to be more rigorous

Susan Mayor LONDON
Researchers and policy makers should make greater use of observational studies to identify environmental and lifestyle causes of disease, a report by leading UK scientists recommended this week. But the design of studies needs to be improved for a better understanding of causal pathways, it says.

The study assessed evidence on the use and interpretation of research in the field, reviewed the literature, and held workshops involving a wide range of stakeholders. “The evidence is clear cut,” the report says. “Environmental influences are both strong and important in the causal processes leading to most common diseases. Nevertheless, the knowledge on the specifics of environmental influences, and of the biological pathways through which they exert their causal effects, is decidedly limited.”

The working group says that priority should be given to high quality research designs that could help identify the environmental components of the causal pathways that lead to disease. This type of observational research can make an important contribution to formulating public health policy and treatment of individual patients, the report concludes. However, policy makers must assess the strength and reliability of evidence before using it to develop public policy.

Identifying the Environmental Causes of Disease: How Should We Decide What to Believe and When to Take Action? is available at www.acmedsci.ac.uk/publications.

UN conference on climate change will test countries’ commitment to public health

Combating the health problems of climate change “must not be at the expense of … tackling existing challenges such as the high burden of disease in Africa”
test countries’ commitment to public health

Rory Watson  BRUSSELS

The 11 day United Nations conference on climate change opening in Bali on 3 December will shed new light on the degree of importance that policy makers attach to public health as they seek ways to mitigate the gradual increase in the world’s temperature and prepare for the consequences.

The final part (a synthesis) of the fourth assessment report of the UN Intergovernmental Panel on Climate Change (IPCC) confirms that the trend towards global warming can no longer be questioned.

“Warming of the climate system is unequivocal, as is now evident from observations of increases in global average air and ocean temperatures, widespread melting of snow and ice, and rising global average sea level,” notes the synthesis, which was released on 17 November (see www.ipcc.ch).

The chapter devoted to health issues confirms that humans are being directly exposed to climate change through new weather patterns and indirectly through alterations in water, air, and food quality and evolving ecosystems. Emerging evidence points to changes in the distribution of some vectors of infectious disease and in the seasonal distribution of some allergenic pollen species.

More specifically, the report predicts with a high degree of confidence that there will be more deaths, disease, and injury from heatwaves, floods, storms, fires, and drought, and greater malnutrition.

The World Health Organization, which produced its first report on climate change and public health 17 years ago, is looking for a strong signal at Bali that the potential effects of extreme weather conditions on humans and health systems will receive greater attention than in the past.

Diarmid Campbell-Lendrum, a senior scientist in WHO’s public health and environment department, said, “WHO would like to see a strong commitment to the need for health protection from climate change, since it will involve additional health risks and extra costs on health services. But this commitment must not be at the expense of continuing our unfinished agenda of tackling existing challenges such as the high burden of disease in Africa.”

Cocaine use rises in Europe while popularity of cannabis reaches a plateau or is falling

Rory Watson  BRUSSELS

Cocaine consumption in Europe is continuing to rise, despite evidence that overall drug use throughout the continent is beginning to stabilise.

The latest annual report from the Lisbon based European Monitoring Centre for Drugs and Drug Addiction, giving data for 2005, says that an estimated 4.5 million Europeans between the ages of 15 and 64 years had taken cocaine in the previous 12 months, whereas the number in 2004 was 3.5 million.

The percentage of cocaine users ranged from 0.1% of the population in Greece to 2% in Italy and the United Kingdom and 3% in Spain. However, the report warns that national averages do not reflect behaviour among young people, mainly males, in urban areas.

It estimates that in 2005 around 13% of people in the UK aged 16 to 29 years who often visit pubs or wine bars used cocaine in the previous 12 months, whereas the percentage among less frequent visitors was 3.7%.

The effect of cocaine use—now the second most widely used illicit drug, after cannabis and ahead of ecstasy and amphetamines—is increasingly being felt in health systems. Almost a quarter (22%) of all new demands for drug treatment in Europe in 2005 were related to cocaine, and the numbers involved (33,027) were nearly three times the numbers seeking treatment in 1999 (12,633).

Cannabis use shows a different trend. Although in 2005 about 23 million adults in the EU reported having tried the drug in the previous 12 months, the indications are that its popularity has reached a plateau or is even falling. Recent data indicate that the percentage of people using it is falling in countries with traditionally high cannabis use, such as Spain, France, the UK, Germany, and the Czech Republic.

Among 16 to 24 year olds in the UK cannabis use fell from 28% in 1998 to 21% in 2005, suggesting that the drug has become less popular among this age group.

However, around three million people (equivalent to 1% of European adults) are thought to take the drug on an almost daily basis.

The report notes that the number of drug related deaths is at an all time high, in marked contrast to the downward trend seen from 2001 to 2003.

In 2005 the number of drug related deaths in the 27 EU countries and Norway was between 7000 and 8000. The deaths were mainly associated with opioid use. Marked rises in the number of deaths were seen in Ireland, Greece, Portugal, Finland, and Norway.

Lung transplants may be harmful in children with cystic fibrosis

A lung transplant is the only remaining therapeutic option for some children with cystic fibrosis. But doctors should warn children and their families that the operation may not be the lifestyle they were hoping for, says an editorial (p 2186). The author was commenting on a “startling” study, which found that transplants were associated with worse, not better, survival for 315 of 514 children placed on a US waiting list between 1992 and 2002.

The researchers used statistical modelling to estimate the effect of surgery on the children’s risk of death. They found that only five of the 514 would (or did) benefit. Just under half the children in the cohort had a transplant. They survived a median of 1037 days after surgery.

The hazard associated with transplantation depended to some extent on other factors, including infection with *Staphylococcus aureus* and age. In this model, surgery didn’t seem to depend to some extent on other factors, including infection with *Staphylococcus aureus* and age. In this model, surgery didn’t seem to be associated with worse, not better, survival for 315 of 514 children placed on a US waiting list between 1992 and 2002.

The study was retrospective and the final follow-up was 566 population controls. Risks were even higher for adults admitted with pulmonary embolism. In two matched cohorts of Danish adults, the 25,199 people admitted with deep venous thrombosis were 1.6 times more likely to have a heart attack (95% CI 1.35 to 1.91) and more than twice as likely to have a stroke during the next year (2.19, 1.85 to 2.60) than 163,566 population controls. Risks were even higher for adults admitted with pulmonary embolism (2.60, 2.14 to 3.14 for heart attack; 2.93, 2.34 to 3.66 for stroke). The association between venous thromboembolism and later arterial cardiovascular events weakened after the first year but remained significant for at least 20 years. Both cohorts came from Danish national databases.

Because venous thromboembolism doesn’t cause heart attacks or strokes, the link between these conditions is probably mediated by a shared risk factor, says a commentary (p 1742). Obesity is the strongest candidate, but diabetes and smoking are also risk factors for both.

Should patients with venous thromboembolism be given drugs to reduce their risk of heart attack and stroke? Not at this stage, says the editorial. We don’t know enough about the mechanisms linking these two previously distinct types of disease.

### Rapid response team reduces mortality in large children’s hospital

On 1 September 2005, a large academic children’s hospital in the US introduced a rapid response team to see and treat children thought to be deteriorating on the general wards. The team aimed to reach them within five minutes. In the 19 months that followed, the hospital wide mortality rate fell by 18% (95% CI 5% to 30%; from 1.01 to 0.83 deaths/100 discharges), the average monthly rate of respiratory or cardiopulmonary arrest outside the intensive care unit fell by 71.7% (2.45 to 0.69 arrests per 1000 admissions), and an estimated 33 lives were saved.

These data may be observational but they provide the most persuasive evidence so far that rapid response teams can work for children as well as adults, says an editorial (p 2311). Any member of staff worried about a child could call the team, which included a doctor, a specialist nurse, a respiratory therapist, and a nurse supervisor. Other possible triggers included suddenly worsening blood pressure, oxygen saturation, or level of consciousness.

It’s impossible to say for certain whether rapid response teams were solely responsible for the improvements. But case mix did not change, and the study’s authors think a direct effect is the likeliest explanation.

### Venous thromboembolism linked to later risk of cardiovascular disease

Danish researchers have found a strong link between hospital admission for venous thromboembolism and later heart attack or stroke. In two matched cohorts of Danish adults, the 25,199 people admitted with deep venous thrombosis were 1.6 times more likely to have a heart attack (95% CI 1.35 to 1.91) and more than twice as likely to have a stroke during the next year (2.19, 1.85 to 2.60) than 163,566 population controls. Risks were even higher for adults admitted with pulmonary embolism (2.60, 2.14 to 3.14 for heart attack; 2.93, 2.34 to 3.66 for stroke). The association between venous thromboembolism and later arterial cardiovascular events weakened after the first year but remained significant for at least 20 years. Both cohorts came from Danish national databases.

Because venous thromboembolism doesn’t cause heart attacks or strokes, the link between these conditions is probably mediated by a shared risk factor, says a commentary (p 1742). Obesity is the strongest candidate, but diabetes and smoking are also risk factors for both.

Should patients with venous thromboembolism be given drugs to reduce their risk of heart attack and stroke? Not at this stage, says the editorial. We don’t know enough about the mechanisms linking these two previously distinct types of disease.

### Haemodilution reduces PSA concentrations in obese men with prostate cancer

Obese men with prostate cancer tend to have lower serum concentrations of the tumour marker prostate specific antigen (PSA) than thinner men. Is it because they are less androgenic—PSA is controlled by testosterone—or is it a simple matter of haemodilution in men with a higher circulating plasma volume? To find out, researchers studied data from three large cohorts of men who had had a radical prostatectomy for cancer in the US. As expected, increasing body mass index was associated with increasing plasma volume
and decreasing serum concentration of PSA preoperatively. But the trend disappeared when the researchers analysed circulating mass (total amount) of PSA instead. In one cohort, obese men actually had a significantly greater mass of PSA than non-obese men. The results, which were extensively adjusted for confounders such as tumour severity and prostate weight, suggest that PSA concentrations are lower in obese men because the protein is diluted in their high plasma volume.

Three quarters of American men over 50 take at least one PSA test, to check for prostate cancer. Many of them are obese and risk falling below the threshold for a biopsy because their serum concentrations of PSA are spuriously low, say the researchers. Late diagnosis could be one reason why obesity is associated with a worse outcome in obese men.

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### Oral vaccine protects European infants from rotavirus gastroenteritis

Rotarix is GlaxoSmithKline’s oral vaccine against rotavirus infections. It worked well in Latin America, and the company has now completed a large phase III trial in nearly 4000 infants in Europe. Two doses of the vaccine given with other routine vaccinations reduced rotavirus gastroenteritis by 87.1% (95% CI 79.6 to 92.1) compared with placebo during one rotavirus season and by 78.9% (72.7 to 83.8) over two seasons. The vaccine also prevented 92-100% of hospital admissions most likely to work for them.


### So many drugs, so little evidence

People with rheumatoid arthritis have plenty of treatment options. But doctors have little good evidence to help choose between them, according to a recent systematic review. After a close examination of nearly 30 years of research (101 studies), the only thing the authors could say with certainty was that no single disease modifying drug was clearly better than any other. The two main groups of disease modifying drugs are the synthetic agents, such as methotrexate and sulfasalazine, and the anti-tumour necrosis factor agents, such as etanercept and infliximab. Used alone, methotrexate had similar clinical effects to the biological agents in this review. Both had similar side effect profiles, although the risks of long term rare or serious side effects are unknown. Combining treatments helped increase the chance of a response in patients who continued to deteriorate despite monotherapy. The evidence was too weak to support one combination over another. Bigger, better, and longer trials that include real world patients are urgently needed, say the authors. These trials should compare different treatment combinations and different treatment strategies directly, collect data on quality of life, and plan for subgroup analyses to help direct patients to the treatments most likely to work for them.


### Back supports reduce back pain among home care workers

People who work in home care have a high prevalence of low back pain. So researchers from the Netherlands thought that these people would be a good target population for a randomised trial of back supports. They recruited 360 workers with a history of back pain from one home care organisation in Rotterdam and allocated 183 of them to use a back support when they had pain or expected to get pain. The rest carried on without the supports, but all participants had their usual yearly session on safe working practices from the company’s in-house health and safety executive. People who used the supports reported nearly 54 fewer days of back pain during the year long study than controls (95% CI –85.2 to –28.7 days each year, P <0.001).

The supports were also associated with a small but significant reduction in pain intensity and disability. But they had no effect on absenteeism. These home care workers took an average of 45 days off sick a year, whether or not they were using a lumbar support. The authors were initially disappointed by this one negative result. But further analysis suggested that because back pain wasn’t a major contributor to absenteeism, back supports were unlikely to get these employees back to work.


### SHORT CUTS

#### EFFECT OF BACK SUPPORTS ON BACK PAIN AND SICK LEAVE

Adapted from *Ann Intern Med* 2007;147:685-92

#### EFFECT OF VACCINE ON ROTAVIRUS GASTROENTERITIS OVER TWO SEASONS

Adapted from *Lancet* 2007;370:1757-63
**BITTER PILLS**

Counterfeit drugs are estimated to represent 10% of the global market in medicines, rising to almost a third in some parts of the developing world. Andrew Jack reports on bids to tackle a growing threat to patients’ health.

When the UK medicines watchdog unveiled its first ever strategy to tackle counterfeiting last week, it was responding to growing concern about the increasingly complex, dangerous, and expanding international traffic in fake drugs. A few weeks earlier, the Medicines and Healthcare Products Regulatory Agency had brought to trial one of the most ambitious prosecutions to date, leading to the imprisonment of four men for handling £1.5m (€2m; $3m) in counterfeits. Other cases concerning still more elaborate schemes are scheduled in the months ahead.

In the past three years, the agency has issued nine withdrawal notices for suspect prescription medicines discovered in the legal distribution chain, compared with just one in the previous decade. Pharmaceutical companies such as Pfizer have been forced into costly withdrawals of batches of their medicines faked by criminals.

**Growing problem**

These incidents are almost certainly an underestimate of the extent of the traffic in counterfeit drugs in the United Kingdom. Although the agency conducts spot checks, it has limited resources to tackle a problem that has been acknowledged only relatively recently.

One indicator is European Union customs statistics, which showed a fourfold increase last year with 497 border seizures of 2.7 million medicines. Although lifestyle drugs such as Viagra dominated, the hauls also included significant numbers of drugs to treat hypercholesterolaemia, osteoporosis, and hypertension. Similar increases have been reported in the United States.

But in Europe and North America, the issue remains modest. The US Food and Drug Administration’s counterfeit drug task force argued last year that extensive oversight meant the problem was still “quite rare,” although it stressed that the drug supply was “increasingly vulnerable to a variety of increasingly sophisticated threats.”

Estimates issued last year by the World Health Organization’s international medicines anti-counterfeiting taskforce (IMPACT), which draws together regulators, manufacturers, police, and other specialists, suggested that fakes represented less than 1% of all medicines in the industrialised world. However, it said that around 10% of the global market was fake, rising to 30% in some parts of the developing world. A recent analysis of artemisinin group drugs for malaria in Kenya and Congo showed nearly a third were fake, rising to 77% for injectable forms.

**Health dangers**

The public health effect is clear. Poor quality medicines cause harm by neglect because patients unwittingly take drugs that lack active ingredients. They may also be active killers, if they contain toxic elements and impurities as a result of cheap ingredients, unhygienic manufacture, or lack of rigorous cleaning between different production batches.

The situation is complicated by the fact that counterfeit drugs often contain active pharmaceutical ingredients, if only because producers are keen to both avoid detection and generate repeat business. The drugs they make may be ineffective and dangerous but difficult to spot because they use active ingredients from a similar class of medicine—swapping a patented statin for a cheaper generic form, for instance.

Other fakes contain the correct ingredients but in the wrong proportions or combinations, for reasons of cost or poor quality control. Apart from the negative consequences for individual patients’ health, this can trigger broader community-wide resistance.

Counterfeiting also has an important commercial impact. It undermines the margins of legitimate drug companies, reducing the profits available for reinvestment in new drugs and for low cost, high quality generics. It cuts the tax revenues paid by these companies.
which governments can use to strengthen health systems.

Fake drugs risk damaging the reputation of drug companies, because well established brands are usurped, damaging public confidence in particular medicines or entire product ranges. Suppliers are therefore often reluctant to publicise incidents of counterfeiting of their products.

Counterfeiting has grown in part because of the high margins it offers to criminal groups, and the relatively low penalties and risks of getting caught. Enforcement has been modest, with scant political will or resources, in part because most public health scares do not take place in the developed world.

The complexity of international counterfeiting networks—which often involve production in China and India, shipment through free trade zones and countries like the UK with a good reputation, and sale through offshore distribution centres—creates particular challenges in coordinating different national police and customs services.

The internet has also helped counterfeiters, boosting the scope to market drugs anonymously by playing on peoples’ desires to reduce costs and circumvent doctors’ opinions by buying directly online through networks that are difficult to supervise.

**International response**

Rising concern has spawned initiatives such as the WHO taskforce, while both the International Narcotics Control Board and the Organisation for Economic Cooperation and Development have flagged up the problem this year.10 The European Parliament and the Council of Europe are considering new regulations, and some developing world regulators like Nigeria’s Nafdac are seeking an international treaty.11

In 1992 the US passed legislation requiring medicines to have a “pedigree” so that they can be tracked through the supply chain, as a way to identify health problems, assist with product recalls, monitor post-launch drug safety, and gather data that could lead to the prosecution of counterfeiters. But practical problems have repeatedly pushed back guidelines and their implementation.

With legal pressure and industry appetite growing, however, a mini-industry to tackle counterfeiting has grown up. Some companies offer sophisticated scanning devices to detect pharmaceutical ingredients at the border. As part of its corporate social responsibility programme, Merck KgA produces a portable laboratory to test drugs.

Much of the debate focuses on “track and trace” technology—systems to identify genuine medicines in the supply chain.12 Although a range of sophisticated approaches have been proposed, including holograms and concealed codes printed on pills, well established methods such as radio frequency identification and two-dimensional bar codes are receiving the most attention.

There have been concerns that radio frequency identification is not always reliable, but a consensus seems to be emerging that it could be used to identify large batches throughout the distribution chain. Individual medicine packets would each be marked with a barcode that pharmacies could read using their existing equipment.

The system would require each packet to have a unique identification number that was standardised across manufacturers and consistent between countries. If the unique barcode number was ever identified more than once, had not been issued, or did not conform to the standard format, the fake would be identified.

Such a system still raises concerns, including individual patient privacy, competitive sensitivity, and the security of the database to prevent unauthorised access. But initial pilots in Belgium, a country that already has identifying numbers to help with social security reimbursement and limit fraud, have showed promise in flagging up drugs subject to recalls as much as counterfeits.13

On a global scale, practical issues with systems to stop counterfeiting remain. The biggest problem is in the developing world, where resources are limited, poor control mechanisms exist, and many medicines are supplied outside conventional, well regulated, developed world pharmacies and doctors’ networks.

Technology in such locations can only be a partial solution. Advocates call for far tighter international coordination, greater funding, greater scrutiny of trans-shipment points, tougher penalties, and patient education to warn of the dangers of unregulated internet sales. There are also broader challenges. Several drug companies have conflated counterfeiting with “diversion” of medicines from Canada, where they are priced more cheaply, to the United States; and the similar practice of “parallel trade” exploiting price differences within the EU. Such trading of medicines may be open to criticism on economic grounds, but where it is legal and regulated, there is scant evidence that it has led to counterfeits entering the legitimate medicines supply chain.

Despite such debates over definitions, counterfeiting is undoubtedly becoming an increasing concern, and a threat to patient health, especially in the developing world.

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**Enforcement has been modest, with scant political will or resources, because most public health scares do not take place in the developed world**
LEARNING THE SECOND WAY

Universities have been developing online learning facilities for doctors and medical students for many years. Now they are turning to the virtual world of Second Life, reports Daniel Stott

Not many lecturers would appreciate their students flying into lecture theatres dressed as cybergoths, but since September Coventry University has begun to encourage such behaviour. The university is pioneering an MSc course in clinical management that holds problem based learning groups for students in Second Life, an online virtual world. The course trains students in managing healthcare facilities and is the first healthcare course to use Second Life as a learning platform.

Second Life is an internet based application that uses three-dimensional graphics to represent an online environment. Users may register for free, adopt a character (known as an avatar) from an online menu, and then explore the virtual world of Second Life. Not only are avatars able to interact with each other through on-screen dialogue boxes—and more recently voice recognition—but they can also create new buildings and online facilities using Second Life’s simple programming tools. Users are also able to create islands—online territories that are separate from the environment’s “mainland” and can have restricted access through passwords.

Other medical schools are beginning to follow Coventry’s lead and are developing modules and courses using Second Life. St George’s Medical School, part of the University of London, for example, is looking at ways in which Second Life can be used to help students interact with patients in a safe, simulated environment. Emily Conradi, the school’s electronic projects manager, also predicts that Second Life has the potential to “enable students from all over the world to gather and hear from expert speakers who could be based anywhere in the world.”

Maggi Savin-Baden, professor of higher education research at Coventry University, thinks that Second Life has advantages over traditional types of distance learning: “Students get a greater sense of being in the same room or the same space as other participants in the process. It’s more active.”

At Coventry University’s Second Life island, 10 students are being employed to build learning facilities for the new intake of Second Life learners.

HOW UNIVERSITIES ARE USING SECOND LIFE

• The University of Nottingham is researching bullying. About 50 avatars have taken part in interviews monitored in Second Life by an occupational psychologist

• The University of Plymouth and Thomas Jefferson University in the United States have developed a sex education zone featuring films about HIV and a stand with current sexual health news

• Cornell University is conducting research into post-traumatic stress disorder, measuring the physiological responses of veterans of the Iraq war and previous Gulf war while participating in a virtual tour through a combat scenario

• Imperial College, London, has a Second Life version of their real world Sir Alexander Fleming building, complete with teleport signs to the library and lecture theatres

Hospital life, but not as we know it: above, an intensive care unit; right, a patient waiting room; and below, a patient with healthcare staff

Potential applications

At Cornell University, New York state, academics have pioneered the use of virtual reality for a range of psychiatric problems. People with phobias of flying, for example, can experience a virtual flight without leaving the safety of the consultation room. Using a computer headset, the patient is exposed to an ascending hierarchy of fear inducing
experiences, from taking a cabin seat with the engines off, to descending and landing in bad weather.

A similar intervention involves virtual public speaking, in which the therapist can control the responses of a virtual audience, ranging from ringing applause to an atmosphere of deep boredom and agitation.

At Idaho State University researchers have designed a Second Life learning environment incorporating two islands, Asterix and Obelix. Dr Ramesh Ramloll, one of the programmers who designed the islands, explains the attraction of learning in Second Life: “It engages people in a way that traditional methods don’t. Also, using Second Life costs dramatically less than designing your own virtual reality environment from scratch, and building environments in Second Life is a collaborative exercise with people who are experts in whatever field you want to learn about.”

Recent exercises conducted on Idaho’s islands include a “pavement triage” pandemic flu disaster, during which doctors attended to infected patients on the streets surrounding a virtual hospital. Participants were able to plan disaster responses in online meetings and were able to use emergency equipment, such as triage tents, which had been designed and programmed to closely mimic real world facilities. “Teams of players on Second Life would be told on-screen that some sort of disaster was unfolding,” explains Dr Ramloll.

“They would then have to collect their uniform, and by clicking on their vests, they would be told what their responsibilities were and the name of the person they would have to answer to during the exercise. “Another recent exercise involved practicing evacuation drills for the Elks Rehabilitation Hospital here in Idaho using a simulation constructed on Second Life.” Dr Ramloll explains that you can get people from different agencies networking and sharing ideas in these exercises. “One of the things that we’ve been working on is getting people from different roles speaking to each other in ‘plain text’ on Second Life—so that involves cutting out a lot of the code numbers and acronyms that might be well understood in one organisation but meaningless to others,” he says.

Pitfalls

Using virtual reality as a learning application does, of course, pose potential problems as well as having possible advantages. Professor Savin-Baden recalls how during one Second Life tutorial “a scantily clad young lady turned up and asked if she was at a nightclub.”

Access to university islands can, however, be locked by administrators, meaning unwanted guests can, in theory, be kept out. Professor Savin-Baden says that some students are initially lukewarm about the idea of having an element of their course being conducted in Second Life. Students without experience of the virtual world are given tuition in easy tasks, she explained.

Cost is another potential stumbling block: maintaining and programming environments in Second Life may be cheaper than designing virtual solutions from scratch, but the costs can still be considerable. In addition to the £6000 (€8600; $12 500) paid for Coventry University’s island, Professor Savin-Baden says that a further £20 000 has been spent on programming. Costs are also associated with making sure that computers on campus are powerful enough.

There is some debate about whether spending money on virtual learning platforms is worthwhile, but some university marketing departments have already spotted the potential that having a virtual presence offers in terms of college branding and attracting future generations of computer literate and Second Life savvy students.

Hamish MacLeod, senior lecturer on the MSc in e-learning course at Edinburgh University explained, “I have had one or two inquiries about the masters course from prospective students who have made a point of visiting Holyrood Park [Edinburgh University’s Second Life campus] before getting in touch—a hint that Second Life can play a role in recruitment.”

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I’d like to make a sage prediction, seeing as it’s early December. One of the joys of watching bad science coverage in the media—as I have done for four years now—is that you start to spot patterns: and this year, just like every Christmas, as regular as mince pies, I can confidently predict a specific rash of stories: they will explain solicitously that chocolate is good for you—“actually”—and red wine is even better.

It’s not much of a prediction, since in the world of public relations, Christmas has started already. “Choxi+” is milk chocolate with “extra antioxidants,” and the newspapers are fawning over it already: “too good to be true,” says the Daily Mirror; “chocolate that is good for you, as well as seductive,” says the Daily Telegraph. The company is said to “recommend” two pieces of its chocolate a day. “Guilt free,” says the Daily Mail: it’s “the chocolate bar that’s ‘healthier’ than 5lb of apples.” Meanwhile, Sainsbury’s is promoting Red Heart wine—with extra antioxidants—as if drinking the stuff was a duty to your grandchildren.

These products represent triumphs of over-extrapolation from observational data, and laboratory hunches. A huge amount has been made of the j-shaped curve in the relationship between alcohol or wine consumption and good health. Moderate drinkers, the media love, are specifically informed, come out better on all kinds of health measures, and nobody wants to ruin Christmas by mentioning confounding variables again (like how moderate red wine drinkers hang out at home with their friends eating salad and talking about their posh jobs and stable social support). A fairy tale science story must be simple, reductionist, and mechanistic. Red wine is good for you because it contains life-giving molecules, like antioxidants.

And nobody wants to spoil Christmas—for the whole family—by mentioning that the antioxidants story is one of the great unspoken non-starters of 20th century medical research. People who eat fresh fruit and vegetables have lots of positive health outcomes, including reduced rates of heart disease and cancer; and fresh fruit and vegetables contain lots of antioxidants; and people who have high levels of antioxidants in their blood seem to be healthier.

There’s even a charming fable from the metabolic flow charts in biochemistry textbooks about what antioxidants do in the body. Sainsbury’s loves that story, along with the others: “Exposure to UV rays, pollution and smoking produces free radicals,” it says. “Free radicals are compounds that cause cell damage, which in the long term can damage health.” It’s such a gloriously simple tale of right and wrong you can almost picture it, in animated form, on ITV after the Queen’s speech. “Antioxidants help counteract the harmful effects of free radicals. Red Heart has an antioxidant level which is 32% higher than the average level of other leading red wines.”

Only a malevolent Scrooge-like figure, mumbling over his glass of tap water in the corner, would dare to point out that if you are going to pore over a biochemistry textbook, and pick pathways out at random, then you can prove anything you like. Phagocytic cells build a wall around invading pathogens and then use free radicals—among other things—to kill the bacteria off. Should we be selling free radical supplements to help people fight infections?

The antioxidant story took a bit of a blow, of course, when people started to do placebo controlled randomised trials with antioxidant vitamin supplements, to see what happened: because overall they seem to do nothing, or at worst, reduce life expectancy. And that’s when you might start to think, well now, perhaps people who eat fresh fruit and vegetables are, just like the people who drink red wine in decorous moderation, living healthily in all kinds of ways. Much like the people who buy vitamin pills. Lusty walks around country mansions. Cycling to work. That kind of thing.

Of course there may yet be something valuable in the antioxidant story, although it’s probably not going to be as simple as dismissing them out by the spoonful. And of course observational studies aren’t inherently evil or useless: they’re frequently fascinating, as part of a puzzle. These are all interesting theoretical research findings, as we try to puzzle out the roots of cancer and heart disease.

But they make a pretty thin excuse for flogging chocolate and alcohol. And somewhere out there—right now—a researcher is rubbing their hands with glee, poring over a press release, picturing themselves in the Today programme studios, planning some choice quotes for the Daily Telegraph: something racy about mince pies cutting heart disease because of the raisins, perhaps, or red wine helping you run faster. Well, it’s Christmas. Have another.

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When a drug causes adverse effects, do the people affected need the help of media pressure to support their claims to compensation? This is certainly true in the case of thalidomide, Germany’s worst ever pharmaceutical tragedy, which started in 1957. Its 2700 survivors in Germany were almost forgotten until a two part television drama named after the drug’s German trade name, Contergan, was broadcast during prime time on 7 and 8 November, highlighting their fate and reaching millions of people. Several accompanying documentaries, interviews, and talk shows have provided additional information.

More than 50 years later, Sebastian Wirtz, chief executive officer of the pharmaceutical firm Grünenthal (the German manufacturer of thalidomide) and grandson of its founder, was the first member of his family prepared to meet people affected by thalidomide, which caused severe malformations in more than 12000 newborns worldwide. Wirtz admitted a “moral responsibility, but no moral fault of Grünenthal” in one of his rare newspaper interviews in the Aachener Zeitung and said that he would not be blackmailed into providing further compensation.

The original DM100m compensation fund was exhausted long ago and left those affected with severe complications with a maximum state sponsored compensation of about €500 (£360; $740) a month. In the United Kingdom and Sweden, where thalidomide had been licensed by other firms, more substantial compensation is provided. Grünenthal is still a privately owned drug company, and has an annual turnover of €800m.

The image of Grünenthal has suffered badly in the past weeks, and the firm’s misguided communication policies have probably increased the damage. In the past two years Grünenthal has concentrated on trying to persuade the court to stop the broadcast of the original version of the film Contergan, or at least require the film’s producers to alter several scenes which the firm said were fictional, therefore not true to historical reality, and showing the firm in a bad light (BMJ 2007;334:933). In summer 2007, the court decided that the film could be shown but with a disclaimer insisting that it is a work of art rather than a documentary of the Contergan scandal. Some scenes in the screenplay had to be changed according to the wishes of Grünenthal.

In the film, lawyer Paul Wegener and his wife Vera, living in economically thriving postwar Germany, receive a shock when their daughter is born without arms and only one leg. The baby into care immediately. In the film, lawyer Paul Wegener and his wife Vera, living in economically thriving postwar Germany, receive a shock when their daughter is born without arms and only one leg. The baby into care immediately. “What’s the matter? Show me the baby,” says Vera after the birth. Hospital staff react by calling the deformed baby “horrible” and advising the parents to put the baby into care immediately. But the couple take on the challenge and soon suspect a link with Contergan, a popular and allegedly harmless sleeping pill, of which Vera had taken just a single pill during her pregnancy. Together with a paediatrician who has found epidemiological evidence for Contergan’s teratogenic effects, Paul Wegener forces the firm Grünenthal into a legal case—after a long courtroom battle the case was settled when Grünenthal established a voluntary fund of DM100 million.

The film shows how difficult it is for a young couple to cope with the strain of bringing up a stigmatised, handicapped child. It has been widely praised for its detailed portrayal of Germany in the 1950s and 60s and its suspense and personal depth, as well as brilliant acting, especially by the young Denise Marko, who, due to a rare genetic disease, has malformations identical to those caused by Contergan. Germany’s most popular television award, the Bambi, will be given to Contergan at the end of the month, and several European countries have either bought the television rights or, like the UK, have shown strong interest in the film.

Grünenthal is continuing its legal battle to challenge historically incorrect scenes in the film in higher courts. Sebastian Wirtz said in the Aachener Zeitung that he stands by his decision to fight for historical truth because television audiences cannot decide between fiction and history. The company website (www.grunenthal.com) has a detailed summary of events. Wirtz continues to refuse to appear in TV talk shows like those accompanying the broadcasting of the film because he considers their atmosphere to be too emotional. A meeting with Contergan victims will take place only if there is no media attention.

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Competition in a publicly funded healthcare system

Are the UK and other countries right to adopt a market based model for improving their health services? Steffie Woolhandler and David Himmelstein believe that the appropriate response to the US experience with such policies is quarantine, not replication.

Why would anyone choose to emulate the US healthcare system? Costs per capita are about twice the Organisation for Economic Cooperation and Development average. Forty seven million people are completely uninsured. Many others with insurance face high out of pocket costs that hinder care and bankrupt more than a million annually.1 Mortality statistics lag behind those of most other wealthy countries, and even for the insured population, clinical outcomes and patient satisfaction are mediocre.2 3

This dismal record arises, we contend, from health policies that emphasise market incentives. Even as the public share of health spending in the US has risen to 60% (box) investor owned firms have eclipsed the public, professional, and charitable bodies that previously managed the financing and delivery of care. The development and effect of US policies that mix public funding and private management has wider relevance because politicians in Europe and beyond are pushing analogous schemes.

Failure of private contracting in Medicare
The combination of tax funding and market oriented delivery is exemplified by the US Medicare programme, which has a budget more than double that of the entire NHS. Until 1965, many US employers offered private health cover, but elderly, poor, and disabled people were mostly uninsured and forced to rely on threadbare government institutions or charity. In 1965, Congress established the Medicare social insurance programme for elderly people. Private hospitals gained a vast new market, and investors soon took note, launching for-profit chains that now account for 15% of US acute care hospitals. Similarly, for-profit dialysis firms rushed in after the government made everyone with end stage renal disease eligible for Medicare in 1972.

Until the 1970s, private insurers (mostly founded and controlled by doctors and hospitals) and Medicare exerted minimal oversight of care and payment rates. But soaring costs prodded employers and government to assert more control. In the private sector, managed care and health maintenance organisations (HMOs)—most of which were controlled by investors rather than health providers and vigorously intervened in clinical care—rapidly gained a foothold.

In the mid-1980s, Medicare also began encouraging elderly people to enrol in private HMOs. Government paid the private plans a fixed monthly premium for each person who switched from traditional (fee for service) Medicare, with the HMO taking over responsibility for purchasing (or, rarely, providing) care. This arrangement was touted as a means to bring market efficiency to the public programme and to broaden patients’ choices.

Unfortunately, the first crop of Medicare HMOs yielded mainly scandal—for example, a major political donor whose plan enrolled thousands of aged patients in Florida (and collected tens of millions of government dollars) but neglected to contract with doctors or hospitals to care for them. He fled prosecution, eventually seeking refuge in Spain.4

Subsequently, Medicare applied stricter regulations. The government set the HMOs’ payment at 95% of the average monthly cost of care for a patient in traditional Medicare, with the expectation of 5% savings through improved efficiency. Patients who chose an HMO—attracted by free spectacles, lower copays, and other benefits not covered under traditional Medicare, with the HMO taking over responsibility for purchasing (or, rarely, providing) care. This arrangement was touted as a means to bring market efficiency to the public programme and to broaden patients’ choices.

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HMOs recognised an opportunity in the skewed distribution of health costs. Most patients use little care—indeed 22% of elderly people cost Medicare nothing at all each year—while the fraction who are severely ill account for the lion’s share of expenditures. Astute HMO executives quickly realised windfall profits through cherry picking—recruiting healthier than average older people who brought hefty premiums but used little care—and returning sick patients, and their high medical bills, to the traditional Medicare programme—disrupting care for millions.5

HMO marketing departments devised selective

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**Tax financed health spending in US**

- Official figures for 2005 peg government’s share of total health expenditure at 45.4%, but this excludes:
  - Tax subsidies for private insurance, which cost the federal treasury $188.6bn (£92bn; €129bn) in 2004 and predominantly benefit wealthy taxpayers
  - Government purchases of private health insurance for public employees such as police officers and teachers. Government paid private insurers $120.2bn for such coverage in 2005: 24.7% of the total spending by US employers for private insurance
  - Government’s true share amounted to 9.7% of gross domestic product in 2005, 60.5% of total health spending or $4048 per capita (out of total expenditure of $6697)
  - By contrast, government health spending in Canada and the UK was 6.9% and 7.2% of gross domestic product respectively (or $2337 and $2371 per capita)
  - Government health spending per capita in the US exceeds total (public plus private) per capita health spending in every country except Norway, Switzerland, and Luxembourg

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recruitment schemes to attract healthy people. These included free fitness club memberships, complementary recruiting dinners at times and places inaccessible to frail elderly people, and advertisements painted on the bottoms of swimming pools. HMOs used financial incentives to encourage doctors to persuade sick patients to leave the HMO—for example, deducting payments to specialists from the primary care doctor’s own capitation payment. Hence, a general practitioner could raise her income by advising patients needing hip replacement to leave the HMO, and even convince herself that such advice might benefit patients by freeing them of HMO restrictions on the choice of surgeon and hospital.

HMOs concentrated on ensuring convenient and attractive care for the modest needs of healthy (and profitable) older people. Meanwhile, expensive, ill patients fared poorly. Stroke patients, those needing home care, and others with chronic illnesses got skimpy care, had bad outcomes, and fled HMOs. And when all else failed and an HMO found itself saddled with too many unprofitably ill patients in a particular county, executives simply closed up shop in that area and returned the patients to traditional Medicare.

By the late 1990s, private HMOs’ selective enrolment of healthy elderly people and removal of sick people had raised annual Medicare costs by about $2bn. Yet despite this subsidy, HMOs couldn’t effectively compete with traditional Medicare. The burden of administrative costs—about 15% in the largest Medicare HMO compared with 3% in traditional Medicare—was too great to overcome. Many HMOs couldn’t sustain the extra benefits they had offered at the outset to attract members.

As enrolment fell, HMOs lobbied hard for government rescue, and Congress upped their payments. Currently, Medicare pays private plans $77bn annually; the cost of caring for the eight million Medicare members who have switched to HMOs is 12% above the cost of caring for comparable patients in traditional Medicare.

Medicare’s HMO contracting programme, originally touted as a market based strategy to improve the public programme’s efficiency, has evolved into a multibillion dollar subsidy for private HMOs. Moreover, the massive financial power amassed by these firms (largely at government expense) is a political roadblock to terminating this failed experiment.

Is private really better?
Other US experiments in using public money to buy care from private firms have also disappointed. Costs for the private insurance that government purchases for public employees have risen even faster than Medicare’s. According to comprehensive meta-analyses, investor owned renal dialysis centres (funded almost entirely by the special Medicare programme that covers everyone needing long term dialysis) have 9% higher mortality than non-profit centres despite equivalent costs; and investor owned hospitals—which receive most of their funding from public coffers—have 2% higher death rates and 19% higher costs than non-profit hospitals. Despite spending less on nurses and other clinical staff, investor owned hospitals spend more on managers.

If the failings of private contracting in the US are underappreciated, so is the major success story of recent US health policy: the Veterans Health Administration system. This network of hospitals and clinics owned and operated by government was long derided as a US example of failed Soviet-style central planning. Yet it has recently emerged as a widely recognised leader in quality improvement and information technology. At present, the Veterans Health Administration offers more equitable care, of higher quality, at comparable or lower cost than private sector alternatives.

Costs of market forces
Health care’s shift from a public service to a business model has raised costs, partly by stimulating the growth of bureaucracy. The proportion of health funds devoted to administration in the US has risen 50% in the past 30 years and now stands at 31% of total health spending, nearly twice the proportion in Canada. Meanwhile, administration has been transmogrified from the servant of medicine to its master, from a handful of support staff dedicated to facilitating patient care to a vast army preoccupied with profitability.

Recent trends elsewhere indicate that the US experience is not unique. The advent of internal markets sharply increased administrative costs in the UK and New Zealand. The overheads of Canadian private insurers are 10 times higher than those of public provincial health insurance programmes. In Australia, tax subsidies for private insurance have directed money through private firms, whose overhead is 12% (versus 3.5% in the public programme); the private hospitals favoured by current policies are about 10%
costlier than public ones. As Germany’s insurance plans have adopted an increasingly business-like mode of operation, administrative costs have soared, rising 63.3% between 1992 and 2003; meanwhile doctors complain about an avalanche of paperwork.

Two factors are at work. Firstly, fragmenting the funding stream, with multiple payers rather than a single government one, necessarily adds complexity and redundancy. Secondly, high administrative costs are intrinsic to the commercial mode (in medical care as elsewhere). Each party to a business transaction must maintain its own detailed accounting records, not primarily for coordination but as evidence in case of disputes. Moreover, investors and regulators demand verification by independent auditors, generating yet another set of records. Thus the commercial record replicates each clinical encounter in paper form before, during, and after it takes place in the examining room. The sense of mutual obligation and shared mission to which medicine once aspired becomes irrelevant, even a liability. Hence, the decision to unleash market forces is, among other things, a decision to divert healthcare dollars to paperwork.

**Market failure**

Market theorists argue that although competition increases administration, it should drive down total costs. Why hasn’t practice borne out this theory?

Investor owned healthcare firms are not cost minimisers but profit maximisers. Strategies that bolster profitability often worsen efficiency. US firms have found that raising revenues by exploiting loopholes or lobbying politicians is more profitable than improving efficiency or quality. Columbia/Hospital Corporation of America (HCA)—the biggest US private hospital operator—deliberately submitted inflated bills and expenses to the government, structured business deals so that Medicare picked up the cost of corporate expenses, and paid doctors in return for patient referrals. Tenet, the second largest hospital firm, has a long history of legal problems. In the 1980s (when the firm was known as National Medical Enterprises) it gave doctors kickbacks to boost referrals and improperly detained psychiatric patients in order to fill beds, resulting in legal settlements totalling nearly $700m.

More recently, Tenet paid hundreds of millions of dollars in fines to resolve claims that it offered kickbacks for referrals; claimed excessive sums from Medicare; and that its hospitals performed hundreds of unnecessary cardiac procedures.

For-profit executives’ incomes also drain money from care. When Columbia/HCA’s chief executive officer resigned in the face of fraud investigations into the company, he left with $324m in company stock. Tenet’s chief executive exercised stock options worth $111m shortly before resigning under pressure from investors in 2003. The head of HealthSouth (the dominant provider of rehabilitation care, mostly paid for by Medicare) made $112m in 2002, the year before his indictment for fraud (charges of which he was later acquitted) and four years before his conviction on unrelated bribery charges.

Even chief executives of untainted firms have reaped enormous rewards. Former Harvard geriatrician John Rowe earned $225,000 a day (including Sundays and holidays) in his 65 months running Aetna health insurance company. Bill McGuire made $1.6bn after giving up pulmonary medicine to run UnitedHealthcare.

While private contracting has benefited executives and shareholders, it has increased costs and worsened quality because health care cannot meet the fundamental requirements for a functioning market. It is fashionable to view patients as consumers, but seriously ill people (who consume most care) cannot shop around, reduce demand when suppliers raise prices, or accurately appraise quality. They necessarily rely on their doctor’s advice on which tests and treatments to “purchase.”

Even for sophisticated buyers like government, the “product” of health care is notoriously difficult to evaluate, particularly since doctors and hospitals create the data used to evaluate and reward them. When Tenet hospitals did heart surgery on healthy patients, the surgical outcomes appeared first rate. Even for honest firms, careful selection of lucrative patients and services is the key to success. Conversely, meeting community needs often threatens profitability and hence institutional survival. In the past decade 425 emergency departments—magnets for both very sick and uninsured patients unable to pay—have closed. Overcrowded US emergency departments turn away an ambulance once a minute, on average.

Finally, a real market would require multiple independent sellers, with free entry into the marketplace. Yet many hospitals exercise virtual monopolies; half of Americans live in regions too sparsely populated to support real medical competition.

### Hallmarks of market based reforms

- Market reforms aim to bring medicine into the realm of commerce, where commodities (homogeneous goods or services) are bought and sold for profit
- The first stage of this process is to divide the medical enterprise into discreet, saleable units (commodities), creating buyers and sellers—for example, separating responsibility for financing and providing care or moving from global hospital budgets to fixed payment for a specific procedure
- Once medical commodities are defined, the sellers (medical providers) are forced to compete, giving rise to financial winners and losers
- Because most medical commodities are heterogeneous (patients differ) providers can gain advantage by market segmentation—for example, caring for a relatively healthy subgroup of patients with a particular diagnosis
- Profitable providers attract investors and amass the financial (and political) power to expand their opportunities, while unprofitable ones are driven from the market

### What’s driving privatisation?

Evidence from the US is remarkably consistent; public funding of private care yields poor results. In practice, public-private competition means that private firms carve out the profitable niches, leaving a financially depleted public sector responsible for the unprofitable patients and services. Based on this experience, only a dunce could believe that market based reform will improve efficiency or effectiveness. Why do politicians—who are anything but stupid—persist on this track?
Such reforms offer a covert means to redistribute wealth and income in favour of the affluent and powerful. Privatisation trades the relatively flat pay scales in government for the much steeper ones in private industry; the 15-fold pay gradient between the highest and lowest paid workers in the US government gives way to the 2000:1 gradient at Aetna.

But even more important, privatisation of publicly funded health systems uses the public treasury to create profit opportunities for firms needing new markets. US private insurers used to focus on selling coverage to employer sponsored groups and shunned elderly people as uninsurable. Now, with employers cutting health benefits, insurers have turned to public treasuries for new revenues. And why stop at selling insurance? Why not tap into the trillions spent annually on care in hospitals and doctors’ offices?

Lessons for other countries
Market fundamentalists conjure visions of efficient health markets partnered with government oversight and funding to assure fairness and universality. But regulation is overmatched. Incentives for optimal performance align imperfectly, at best, with the real goals of care. Matrices intended to link payment to performance on trust and common purpose; and leadership not by institutions with health priorities and stimulate cooperation, but rather that of profit-maximizing corporations, growing; those who guilelessly pursue the arduous work of good patient care lose in the medical marketplace.

Lessons for new revenues. And why stop at selling insurance? "It is the infernal machinery of profit that produces necessity, and the necessity of profit that brings about the world.

Commercialisation drives up costs by diverting money to profits and fueling growth in management and financial bureaucracy. The poor performance of US health care is directly attributable to reliance on market mechanisms and for-profit firms and should warn other nations from this path.

SUMMARY POINTS
The US has long combined public funding with private healthcare management and delivery. Extensive research shows that for-profit health institutions provide inferior care at inflated prices.

US experience shows that market mechanisms undermine medical institutions unable or unwilling to tailor care to profitability. Commercialisation drives up costs by diverting money to profits and fueling growth in management and financial bureaucracy. The poor performance of US health care is directly attributable to reliance on market mechanisms and for-profit firms and should warn other nations from this path.


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Future of quality measurement

General practitioners have responded well to current UK performance targets. Helen Lester and Martin Roland examine the options for keeping up the progress

In the past decade there has been sustained international interest in measuring quality of care. In the United Kingdom, quality indicators with financial incentives to reward good care were introduced as a result of increasing awareness of variable quality in primary care, the technical feasibility of introducing evidence based indicators within information technology systems, and a resolve by political negotiators to use improved quality to secure additional investment in primary care. Similar but less comprehensive initiatives have been introduced in the United States, Europe, Australia, and New Zealand. However, as this series has shown, the use of quality measures has also created controversy. Our view is that using incentives to improve quality of care has been beneficial. We look at what needs to be done to ensure those benefits remain in the future.

Options for developing quality measures

The quality and outcomes framework, which forms the basis of quality measurement in UK primary care, could be developed in several different ways:

- Leave indicators unchanged and expect higher achievement each year—This means restricting the potential benefits of quality measures to a limited number of areas
- Add new indicators or conditions regularly—This could lead to a vast and unmanageable set of measures
- Build a larger set of evidence based measures that are all monitored and pay for performance against a subset of these

- Remove measures once a predetermined and agreed level of achievement has been reached—Although this would allow new measures to be introduced without making the scheme unmanageable, it would require robust information about the effect of removing measures on performance in terms of both patient care and practice income and agreement over reintroduction of measures if performance worsens
- Rotate measures regularly, enabling a potential improvement across a range of conditions and areas—This would be our preferred option, although it would need to be carefully piloted to look for and guard against unintended consequences to patient care or practice morale.

The quality measures introduced into general practice in 2004 were mainly drawn from existing national guidelines. They reflected widely accepted standards of clinical care, and there was little direct criticism of the indicators themselves. The first major revision, in 2006, included evidence based indicators that changed clinical practice in ways that were unfamiliar to many general practitioners—for example, encouraging use of validated structured questionnaires as part of the assessment of patients with depression and more active management of chronic kidney disease. Indicators that seek to extend existing practice will always be more controversial than those reinforcing established practice. In our view, indicators that aim to change standard practice should be particularly carefully evaluated, both before and during their introduction. Piloting of new measures for at least 12 months would highlight any professional concerns, education and training needs, and information technology problems.

Interpersonal aspects of care

A common criticism of quality measures is that they look at only limited areas of clinical practice and ignore, and hence may devalue, some core aspects of general practice. These aspects include care for people with multiple complex problems, care for people for whom continuity of care makes a real difference to satisfaction, and the quality of interpersonal care itself. Current UK quality measures may discourage continuity of care, for example by fragmenting care between doctors and nurses, and there is certainly an argument that something in the organisation and financing of general practice should encourage continuity of care. Indeed, there is urgency here, since it may not be long before the trainers within primary care are doctors who have grown up in a climate that prizes the easily measurable and financially

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This is the last article in a series looking at use of performance indicators in the UK and elsewhere. This series is edited by Azeem Majeed, professor of primary care, Imperial College London (a.majeed@imperial.ac.uk) and Helen Lester, professor of primary care, University of Manchester (helen.lester@manchester.ac.uk).
rewarded above the less measurable and definable aspects of care.

We also need to place greater value on patients’ views of care when measuring the quality of interpersonal care. However, as Elwyn and colleagues highlighted, it is less clear whether doctors should be paid according to the results of patient questionnaires. Such an approach would cause major problems in practices where patient turnover was high or where patients were unfamiliar with the health system. Research is needed to determine the effect of paying practices against patient evaluation scores and to develop more innovative and meaningful ways of involving patients from different social and ethnic backgrounds in their health care.

Effect of measurement on health inequality
Quality improvement measures targeted at high risk patients should, in theory, reduce health inequalities. When cervical cytology and immunisation targets were introduced in 1990, practices in affluent areas rapidly reached near maximum performance but deprived areas caught up during the next few years. This led to a substantial overall reduction in inequality, an example of the inverse equity hypothesis.

In the quality and outcomes framework, affluent areas achieved higher scores and reported more exceptions than poorer areas, but the differences were small. Overall, the financial incentives seem to have reached areas of high need relatively effectively for most targets. The effect of incentive structures needs to be constantly reviewed to ensure that they deliver health benefits across all communities. An important subsidiary message is the need to take a long term view when interpreting the effects of quality measures on health inequalities.

Learning from beyond medicine
Measuring aspects of quality is now part of 21st century life, and we may be able to learn from other disciplines. Should we, for example, be looking at the business sector’s 15 years of experience from implementing standards such as Investors in People? This voluntary standard has been achieved by over 32000 organisations employing over 27% of the UK workforce. However, when the standard was introduced, its effect was less than predicted since many firms used it to gain recognition for existing good practice. This is perhaps analogous to the many practices in 2004-5 that achieved their quality and outcomes framework targets through accurate recording of existing practice. Would this knowledge have influenced Department of Health predictions about achievement levels in primary care and helped shape the associated financial payments? Such commonalities highlight the importance of looking beyond the immediate and obvious comparators if we want to broaden our understanding of the potential and problems of introducing and developing quality measures.

Financial incentives are, of course, not the only way of improving the quality of care. In the five years before the quality and outcomes framework was introduced, major improvements occurred in the quality of management of chronic disease in general practice. We need to continue to use a mix of professional, financial, and managerial approaches and experiment to find the mix that gives the NHS best value for money and patients the best care.

Contributors and sources: HL has written about pay for performance and has a longstanding research interest in health quality and inequalities. MR is a general practitioner whose research over the past 10 years includes developing ways of measuring and improving quality of care.

Competing interests: MR provided academic advice to the BMA and employers’ negotiating teams on the development of the quality and outcome framework in 2001 and 2002. HL provides this advice to the current negotiating teams.

Provenance and peer review: Commissioned; externally peer reviewed.

8. Investors In People. www.investorsinpeople.co.uk/Pages/Home.aspx

“Write me a sentence”

“I wish I was in the bosom of my family.”

An elderly man whom I’d never met before gave this response when I asked him to “write me a sentence” during a mini-mental state exam. He went on to pour out the story of how his teenage grandson, whom he’d never thought cared for him, had chased the ambulance down the road crying when he was brought into hospital.

Any house officer in geriatrics is painfully familiar with the questions that make up the mini-mental state exam. But what’s often just another routine job from the ward round sometimes becomes much more. I’m sure I’m not the only person who’s had patients write, “I want to go home,” “I’ve had enough,” or, agonisingly, “I wish I was dead.” Sometimes these sentences are the first glimpse of what’s really going on inside.

All this made me think about that other scourge of the house officer, GDS, with its rigid attempts to measure misery. And expecting an 84 year old to tick a box to say that he or she feels worthless rarely seems respectful, with its rigid attempts to measure misery. And expecting an 84 year old to tick a box to say that he or she feels worthless rarely seems respectful.
Implications of prognostic pessimism in patients with chronic obstructive pulmonary disease (COPD) or asthma admitted to intensive care in the UK within the COPD and asthma outcome study (CAOS): multicentre observational cohort study

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ABSTRACT

Objective To determine whether clinicians’ prognoses in patients with severe acute exacerbations of obstructive lung disease admitted to intensive care match observed outcomes in terms of survival.

Design Prospective cohort study.

Setting 92 intensive care units and three respiratory high dependency units in the United Kingdom.

Participants 832 patients aged 45 years and older with breathlessness, respiratory failure, or change in mental status because of an exacerbation of COPD, asthma, or a combination of the two.

Main outcome measures Outcome predicted by clinicians. Observed survival at 180 days.

Results 517 patients (62%) survived to 180 days. Clinicians’ prognoses were pessimistic, with a mean predicted survival of 49% at 180 days. For the fifth of patients with the poorest prognosis according to the clinician, the predicted survival rate was 10% and the actual rate was 40%. Information from a database covering 74% of intensive care units in the UK suggested no material difference between units that participated and those that did not. Patients recruited were similar to those not recruited in the same units.

Conclusions Because decisions on whether to admit patients with COPD or asthma to intensive care for intubation depend on clinicians’ prognoses, some patients who might otherwise survive are probably being denied admission because of unwarranted prognostic pessimism.

INTRODUCTION

Each year in the United Kingdom, around 30 000 deaths are associated with chronic obstructive pulmonary disease (COPD).1 Many patients with exacerbations of COPD benefit from assisted ventilation, but for intubation the patient must be admitted to an intensive care unit. COPD accounts for 3% of such admissions in the UK, with a median stay of 16 days (interquartile range 9-29 days).2

Doctors consider prognosis to be of “paramount importance” in deciding which patients should be admitted to intensive care,3 and admission might be refused.4 Prognosis, however, can be difficult,5 and in an American study doctors’ predictions of survival tended to be pessimistic compared with a prognostic model.7 If prognoses for patients in the UK with exacerbations of COPD are also unduly pessimistic, some patients with reasonable medium term prognoses might be being denied admission to intensive care for intubation and care.

METHODS

We invited all intensive care units participating in the UK case mix programme8 and three respiratory high dependency units to take part. Eligible patients were those admitted to participating units for breathlessness, respiratory failure, or change in mental status because of an exacerbation of COPD, asthma, or a combination of the two.

Participants 832 patients aged 45 years and older with breathlessness, respiratory failure, or change in mental status because of an exacerbation of obstructive lung disease. Patients were excluded if they were aged under 45 years or had had surgery within the past 10 days or had been transferred directly from another hospital to the unit. Data were collected for admissions from March 2002 to September 2003 with follow-up to 180 days after admission to intensive care.

On admission, the admitting doctor was asked to estimate the patient’s probability of survival to discharge from intensive care or high dependency, to discharge from hospital, and at 180 days after admission. We determined actual survival to 180 days from the general practitioner and confirmed this through the Office for National Statistics. Data were also collected on prognostic variables.

Analyses were carried out using Stata version 9 (Stata Corp, College Station, Tx).

RESULTS

Of 239 intensive care units in the UK in January 2002, 177 were contributing to the case mix programme. Of
Similar pessimism is observed in clinical practice and has the potential to distort clinical decision making.

DISCUSSION

Clinicians are generally pessimistic about the survival prospects of patients with exacerbations of COPD and have particular problems in identifying those with poor prognosis. Patients might therefore be inappropriately excluded from intensive care and the chance of intubation on the basis of a false prediction of futility. The units and patients recruited to this study seem to be representative of UK practice.

Limitations

That we recruited only patients admitted to intensive care or high dependency is a clear limitation. The general level of pessimism among those refused admission, however, was likely to have been even greater than in those admitted. We cannot see how it could have been less. Prognostic pessimism was found across a wide range of subgroups by severity and was also found in a US study that was not limited to patients in critical care.

Historically, access to intensive care in the UK has been problematic and it has not always been possible to admit every patient who might benefit. A culture of pessimism might protect clinicians from the cognitive dissonance involved in being unable to intubate patients they knew to have a reasonable prognosis. When renal dialysis was much less available the discussions around withholding it were often accompanied by predictions of futility if it were to be offered. In the context of triage of patients with COPD, however, this pessimism might be distorting decision making.

The evidence for prognostic pessimism was weakest in the following subgroups: age $\geq$ 75 years, mean arm circumference $<$ 25 cm, worst quarter for acute physiology score, and chairbound or bedbound before admission to intensive care or high dependency.

Clinician pessimism was particularly marked for the patients in the lower fifth of the distribution of prognosis (figure). In fact, the tenth of patients with the poorest clinician prognosis had a predicted 180 day survival of around 3% and an actual survival of around 36%.

WHAT IS ALREADY KNOWN ON THIS TOPIC

Simulation studies in the UK have shown that clinicians are pessimistic in predicting survival after admission to intensive care for patients with chronic obstructive pulmonary disease.

WHAT THIS STUDY ADDS

Similar pessimism is observed in clinical practice and has the potential to distort clinical decision making.


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Cancer incidence and mortality in relation to body mass index in the Million Women Study: cohort study

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ABSTRACT
Objective To examine the relation between body mass index (kg/m²) and cancer incidence and mortality.
Design Prospective cohort study.
Participants 1.2 million UK women recruited into the Million Women Study, aged 50-64 during 1996-2001, and followed up, on average, for 5.4 years for cancer incidence and 7.0 years for cancer mortality.
Main outcome measures Relative risks of incidence and mortality for all cancers, and for 17 specific types of cancer, according to body mass index, adjusted for age, geographical region, socioeconomic status, age at first birth, parity, smoking status, alcohol intake, physical activity, years since menopause, and use of hormone replacement therapy.
Results 45 037 incident cancers and 17 203 deaths from cancer occurred over the follow-up period. Increasing body mass index was associated with an increased incidence of endometrial cancer (trend in relative risk per 10 units = 2.89, 95% confidence interval 2.62 to 3.18), adenocarcinoma of the oesophagus (2.38, 1.59 to 3.56), kidney cancer (1.53, 1.27 to 1.84), leukaemia (1.50, 1.23 to 1.83), multiple myeloma (1.31, 1.04 to 1.65), pancreatic cancer (1.24, 1.03 to 1.48), non-Hodgkin’s lymphoma (1.17, 1.03 to 1.34), ovarian cancer (1.14, 1.03 to 1.27), all cancers combined (1.12, 1.09 to 1.14), breast cancer in postmenopausal women (1.40, 1.31 to 1.49) and colorectal cancer in premenopausal women (1.61, 1.05 to 2.48). In general, the relation between body mass index and mortality was similar to that for incidence. For colorectal cancer, malignant melanoma, breast cancer, and endometrial cancer, the effect of body mass index on risk differed significantly according to menopausal status.
Conclusions Increasing body mass index is associated with a significant increase in the risk of cancer for 10 out of 17 specific types examined. Among postmenopausal women in the UK, 5% of all cancers (about 6000 annually) are attributable to being overweight or obese. For endometrial cancer and adenocarcinoma of the oesophagus, body mass index represents a major modifiable risk factor; about half of all cases in postmenopausal women are attributable to overweight or obesity.

INTRODUCTION
The prevalence of obesity has been increasing in developed countries,1 and national survey data from the United Kingdom indicate that around 23% of all women in England are obese and 34% are overweight.2 Obesity is known to be associated with excess mortality from all causes combined,3-5 but less is known about its effects on cancer. In particular, although it is widely accepted that body mass index (BMI) is positively associated with cancers of the colon, endometrium, and kidney, adenocarcinoma of the oesophagus, and postmenopausal breast cancer,6 the magnitudes of such effects and the role of BMI in the development of other, rarer, cancers are less certain. Furthermore, body mass index may affect not only the development of certain cancers but also the subsequent risk of death.7 Examining the effect of BMI on both incidence and mortality within the same population is therefore important. We report here on the risk of incident and fatal cancer for a wide range of malignancies according to BMI among women in the Million Women Study, a large cohort study of women in the UK.

METHODS
Data collection, follow-up, and definitions
In 1996-2001 a total of 1.3 million women aged 50-64 who had been invited for screening for breast cancer at screening centres throughout England and Scotland completed the first study questionnaire, which asked about height, weight, social and demographic factors, and other personal characteristics. The cohort was resurveyed about three years after recruitment to update information on various factors, including weight. Full details of the study design and methods are described elsewhere,8 and both questionnaires can be viewed at www.millionwomenstudy.org. Study participants have been flagged on the National Health Service central registers, so that cancer registrations and deaths are routinely notified to the study investigators. This information includes the date of each such event and codes the site and morphology of the cancer according to the ICD-10 (international classification of diseases, 10th revision). All participants gave their written consent to take part in the study.
At recruitment, we asked women for their current weight and height and then used these variables to derive body mass index (weight (kg)/height (m)^2), which we categorised as follows: less than 22.5, 22.5-24.9, 25.0-27.4, 27.5-29.9, and 30 or more. In all analyses, we chose the BMI category of 22.5-24.9 as the reference group. We defined women with a BMI of 25-29.9 as “overweight” and women with a BMI of 30 or more as “obese,” in accordance with the World Health Organization’s criteria.9

We examined incidence of and mortality from cancer in relation to BMI for all cancers combined (except non-melanoma skin cancer) and for 17 of the most common cancer sites or types of cancer. As some evidence exists to show that adenocarcinoma of the oesophagus may be more strongly related to BMI than squamous cell carcinoma of the oesophagus,6 we subdivided oesophageal cancers into these two histological types on the basis of ICD-10 morphology codes. Similarly, because the effect of BMI on the risk of breast cancer is known to vary according to menopausal status and use of hormone replacement therapy,6 we did separate analyses with respect to breast cancer for premenopausal women and postmenopausal women who had never used hormone replacement therapy.

Statistical analysis
We excluded women diagnosed before recruitment as having any cancer other than non-melanoma skin cancer (C44), or for whom height, weight, or both were unknown, from all analyses. In analyses of cancer incidence, eligible women contributed person years from the date of recruitment until the date of registration with the cancer of interest, date of death, or end of follow-up, whichever was the earliest. In addition, women diagnosed with any cancer other than the cancer of interest (except non-melanoma skin cancer) during the follow-up period were censored at the date of diagnosis of that cancer. The end of follow-up for cancer incidence was 31 December 2004 for all registries except Trent and North Yorkshire, Northwest, and Scotland, for which the corresponding dates were 30 June 2004, 31 December 2003, and 31 December 1999. For analyses of cancer mortality, eligible women contributed person years from recruitment until death from the cancer of interest, death from some other cause, or end of follow-up, whichever was the earliest. The end of follow-up for cancer mortality was 31 December 2005.

We considered each of the cancer sites of interest as an end point in a proportional hazards model with body mass index included as a categorical variable and attained age as the underlying time variable. We stratified analyses by broad geographical region (10 regions corresponding to the areas covered by the cancer registries) and fifths of socioeconomic status (10 regions corresponding to the areas covered by the cancer registries) and made adjustments for age at first birth (<20, 20-24, 25-29, ≥30), parity (0, 1, 2, 3, ≥4), smoking status (never, past, current <10 cigarettes/day, current 10-19 cigarettes/day, current ≥20 cigarettes/day), average daily alcohol intake in drinks per day (0, 1, 2, ≥3), physical activity (rarely/never, ≤once a week, >once a week) and, where appropriate, years since menopause (premenopausal, perimenopausal, <5, ≥5) and use of hormone replacement therapy (current, past, never). Unless otherwise specified, we derived all variables included in the model from information reported at recruitment. We confined analyses of endometrial and cervix cancer to women who reported never having had a hysterectomy and analyses of ovarian cancer to women who reported not having had a bilateral oophorectomy before recruitment. We assigned women with missing

### Table 1 | Characteristics of the study population at recruitment, and details of follow-up, according to body mass index. Values are percentages (numbers) unless stated otherwise

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Body mass index (kg/m²)</th>
<th>≤25</th>
<th>25-29</th>
<th>≥30</th>
<th>All women</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of women</td>
<td>566 738</td>
<td>436 183</td>
<td>219 709</td>
<td>2 222 630</td>
<td></td>
</tr>
<tr>
<td>Median (interquartile range) body mass index</td>
<td>22.9 (21.5-23.9)</td>
<td>27.0 (25.9-28.2)</td>
<td>32.9 (31.1-35.7)</td>
<td>25.4 (23.0-28.6)</td>
<td></td>
</tr>
<tr>
<td>Mean (SD) age (years)</td>
<td>55.7 (4.4)</td>
<td>56.1 (4.4)</td>
<td>56.0 (4.4)</td>
<td>55.9 (4.4)</td>
<td></td>
</tr>
<tr>
<td>Upper third of socioeconomic group</td>
<td>36 (206 743)</td>
<td>32 (141 598)</td>
<td>26 (57 326)</td>
<td>33 (605 567)</td>
<td></td>
</tr>
<tr>
<td>Mean (SD) No of children</td>
<td>2.0 (1.2)</td>
<td>2.2 (1.2)</td>
<td>2.3 (1.4)</td>
<td>2.1 (1.2)</td>
<td></td>
</tr>
<tr>
<td>Mean (SD) age at first birth (years)</td>
<td>24.2 (4.3)</td>
<td>23.7 (4.2)</td>
<td>23.2 (4.3)</td>
<td>23.8 (4.3)</td>
<td></td>
</tr>
<tr>
<td>Strenuous physical activity more than once a week</td>
<td>25 (138 817)</td>
<td>19 (82 030)</td>
<td>14 (29 950)</td>
<td>21 (250 797)</td>
<td></td>
</tr>
<tr>
<td>Mean (SD) alcohol intake (g/day)</td>
<td>5.6 (6.3)</td>
<td>4.9 (6.0)</td>
<td>3.7 (5.4)</td>
<td>5.0 (6.1)</td>
<td></td>
</tr>
<tr>
<td>Current smoker</td>
<td>22 (122 834)</td>
<td>18 (80 058)</td>
<td>16 (34 196)</td>
<td>19 (237 088)</td>
<td></td>
</tr>
<tr>
<td>Current user of hormone replacement therapy</td>
<td>37 (206 861)</td>
<td>33 (143 542)</td>
<td>28 (61 176)</td>
<td>34 (411 579)</td>
<td></td>
</tr>
<tr>
<td>Hysterectomy</td>
<td>22 (126 056)</td>
<td>26 (114 714)</td>
<td>28 (61 870)</td>
<td>25 (302 640)</td>
<td></td>
</tr>
</tbody>
</table>

### Follow-up

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>≤25</th>
<th>25-29</th>
<th>≥30</th>
<th>All women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Woman years of follow-up for incidence (1000s)</td>
<td>3 014</td>
<td>2 276</td>
<td>1 129</td>
<td>6 419</td>
</tr>
<tr>
<td>Total No of incident cancers</td>
<td>20 600</td>
<td>15 890</td>
<td>8 547</td>
<td>45 037</td>
</tr>
<tr>
<td>Woman years of follow-up for death (1000s)</td>
<td>3 976</td>
<td>3 041</td>
<td>1 518</td>
<td>8 536</td>
</tr>
<tr>
<td>Total No of cancer deaths</td>
<td>7 812</td>
<td>5 952</td>
<td>3 439</td>
<td>17 203</td>
</tr>
</tbody>
</table>
values for any of the adjustment variables to a separate category for that variable. We also examined the effect of restricting analyses to women with known values for all adjustment variables and of varying the level of adjustment for certain factors.

We summarised the relation between BMI and incidence for each cancer site or type in the form of a log-linear trend in risk per 10 unit increase in BMI (broadly equivalent to the difference in median BMI among obese women compared with women in the reference category of 22.5-24.9). We did various sensitivity analyses to assess the robustness of these summary estimates under relevant restrictions. Updated information on body mass index from the follow-up questionnaire was available for 450,186 (36.8%) of the women included in these analyses. We therefore did additional analyses using this updated information to estimate median values of BMI within categories defined by BMI at recruitment, to allow for potential regression dilution.11 We also repeated analyses separately for women defined as premenopausal at recruitment and for women defined at recruitment as postmenopausal and never having used hormone replacement therapy, for those sites with more than 50 cases among premenopausal women.

As the analyses presented here generally involve comparison of risks across more than two categories, variances are, where appropriate, estimated by treating the relative risks as floating absolute risks.12 Results according to BMI category are, therefore, presented in the form of plots of relative risks and their corresponding floated confidence intervals. The position

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Relative risk* of cancer incidence for individual cancer sites or types according to body mass index</th>
</tr>
</thead>
<tbody>
<tr>
<td>Site (ICD-10 code)</td>
<td>No of cases</td>
</tr>
<tr>
<td>Adenocarcinoma of oesophagus† (C15)</td>
<td>150</td>
</tr>
<tr>
<td>Squamous cell carcinoma of oesophagus‡ (C15)</td>
<td>263</td>
</tr>
<tr>
<td>Stomach (C16)</td>
<td>521</td>
</tr>
<tr>
<td>Colorectum (C18-C20)</td>
<td>4008</td>
</tr>
<tr>
<td>Pancreas (C25)</td>
<td>795</td>
</tr>
<tr>
<td>Lung (C34)</td>
<td>3171</td>
</tr>
<tr>
<td>Malignant melanoma (C43)</td>
<td>1635</td>
</tr>
<tr>
<td>Premenopausal breast (C50)</td>
<td>1179</td>
</tr>
<tr>
<td>Postmenopausal breast† (C50)</td>
<td>5629</td>
</tr>
<tr>
<td>Cervix (C53)</td>
<td>330</td>
</tr>
<tr>
<td>Endometrium (C54)</td>
<td>2657</td>
</tr>
<tr>
<td>Ovary (C56)</td>
<td>2406</td>
</tr>
<tr>
<td>Kidney (C64)</td>
<td>723</td>
</tr>
<tr>
<td>Bladder (C67)</td>
<td>615</td>
</tr>
<tr>
<td>Non-Hodgkin’s lymphoma (C82-C85)</td>
<td>1509</td>
</tr>
<tr>
<td>Multiple myeloma (C90)</td>
<td>491</td>
</tr>
<tr>
<td>Leukaemia (C91-C95)</td>
<td>635</td>
</tr>
<tr>
<td>Brain (C71)</td>
<td>571</td>
</tr>
<tr>
<td>All cancers (C00-C97, excluding C44)</td>
<td>45 037</td>
</tr>
</tbody>
</table>

FAR=floating absolute risk; FC=floated confidence interval.

*Adjusted for age, geographical region, socioeconomic status, reproductive history, smoking status, alcohol intake, physical activity, and, where appropriate, time since menopause and use of hormone replacement therapy.
†ICD-0 morphology codes 8140/3, 8144/3, 8145/3, 8260/3, 8480/3, 8481/3, 8490/3.
‡ICD-0 morphology codes 8070/3, 8071/3, 8072/3, 8074/3.
§Restricted to never users of hormone replacement therapy.
of the square indicates the value of the relative risk, and its area is inversely proportional to the variance of the logarithm of the relative risk, providing an indication of the amount of statistical information available for that particular estimate. Results in the text that refer to a specific comparison of two BMI categories or to an estimate of trend are presented in the form of conventional relative risks and their corresponding confidence intervals.

For those cancer sites for which we saw a significant trend of increasing risk with increasing BMI, we estimated the attributable proportions of incident disease in postmenopausal women due to being overweight or obese (BMI ≥25) and obese (BMI ≥30) by using adjusted estimators of attributable risk that also take account of possible effect modification. We stratified relative risks of cancer in postmenopausal women used for estimation of attributable risks by smoking status (never smoker, past smoker, current smoker: <15, ≥15 cigarettes/day) and use of hormone replacement therapy (never, past, current). We based estimates of the distribution of postmenopausal UK women within each combination of these factors on the observed distribution within the cohort of women used for these analyses. However, to take account of changes in the average distribution of BMI in UK women of this age that have taken place since the cohort was recruited, we fixed the marginal proportions of women with a BMI of <25, 25-29, and ≥30 at 30%, 39%, and 31% (on the basis of data in women aged 55-74 from the health survey for England 2004\textsuperscript{2}, and we adjusted the proportions within each combination of factors proportionately. We compared estimates of attributable risk obtained by using the above approach with those obtained from the simpler approach that takes no account of effect modification.

**RESULTS**

In total, 1,222,630 women who had not been registered with a cancer (other than non-melanoma skin cancer) at the time of recruitment and for whom BMI could be calculated were eligible for analysis. Among these women, the average age at recruitment was 55.9 years. During an average follow-up period of 5.4 years for cancer incidence and 7.0 years for cancer mortality, 45,037 incident cancers and 17,203 deaths from cancer occurred. For some cancers typically associated with a very short survival time—namely, lung, pancreas, and brain cancer—the number of deaths was larger than the number of incident cases because of the slightly longer period of follow-up for mortality than for incidence. When we compared sociodemographic and lifestyle characteristics of women in three broad categories of BMI, we found that BMI was strongly associated with almost all of the characteristics examined (table 1). In particular, women with higher BMI tended to come from a lower socioeconomic class; were less likely to smoke, drink, and use hormone replacement therapy; and had more children than women with lower BMI.

![Fig 1](bmj.com) Relative risk of cancer incidence and mortality for individual cancer sites or types according to body mass index (22.5-24.9=reference group). Adjusted for age, geographical region, socioeconomic status, age at first birth, parity, smoking status, alcohol intake, physical activity, and, where appropriate, time since menopause and use of hormone replacement therapy. Het=test for heterogeneity across categories of body mass index on df=4. *Restricted to never users of hormone replacement therapy
Table 2 shows the relative risk of cancer incidence for all cancers and for each of the 17 specific sites or types, adjusted for age, geographical region, socioeconomic status, age at first birth, parity, smoking status, alcohol intake, physical activity, and, where appropriate, years since menopause and use of hormone replacement therapy. Table 3 shows corresponding relative risks for cancer mortality. The relations between BMI and cancer incidence and mortality for all cancers combined, and for 11 selected sites, are presented graphically in figure 1.

We found significant heterogeneity in the relative risk of cancer incidence across BMI categories for all cancers \((P<0.0001)\), adenocarcinoma of the oesophagus \((P=0.0009)\), squamous cell carcinoma of the oesophagus \((P<0.0001)\), pancreatic cancer \((P=0.03)\), lung cancer \((P<0.0001)\), postmenopausal breast cancer \((P<0.0001)\), endometrial cancer \((P<0.0001)\), kidney cancer \((P=0.0005)\), and leukaemia \((P=0.0007)\). Although a general test for heterogeneity across the five categories of BMI was not statistically significant for ovarian cancer \((P=0.1)\), non-Hodgkin’s lymphoma \((P=0.2)\), or multiple myeloma \((P=0.1)\), a more directed test of linear trend in the log relative risks with increasing BMI was significant for each of these cancers \((P=0.02\) for each type of cancer).

For most of the sites that showed significant heterogeneity in risk according to BMI, the relative risk of cancer increased with increasing BMI. The exceptions to this pattern were squamous cell carcinoma of the oesophagus and lung cancer, for which we found trends of decreasing risk with increasing BMI \((P<0.0001\) in both cases). As lack of physical activity may be causally related to high BMI, we repeated the analyses in tables 2 and 3 without adjustment for physical activity, but the results were essentially unchanged. We also repeated analyses with inclusion of an interaction term for smoking and alcohol status in the model, but this made little difference to the results. Nor did the results change materially when we restricted analyses to women with complete information for all of the adjustment factors.

In general, the patterns for cancer mortality according to BMI were broadly similar to those for cancer incidence, and most cancer sites that showed a significant trend in the relative risk of incidence with increasing BMI also showed a similar trend in the risk of mortality with increasing BMI. For stomach cancer, colorectal cancer, malignant melanoma, cervix cancer, bladder cancer, and brain cancer, we found no significant evidence of any variation in the overall risk of incidence or mortality according to BMI. Analyses of colorectal cancer risk according to subsite yielded similar results for colon cancer (relative risks in BMI categories <22.5, 22.5-24.9 (reference), 25.0-27.4, 27.5-29.9, and ≥30 were 1.01, 1.00, 1.03, 0.99, and 1.01) and rectal cancer (1.04, 1.00, 1.05, 1.06, and 1.00).

Figure 2 presents, in order of decreasing magnitude, the estimated relative risk of cancer incidence associated with an increase of 10 units in BMI for each individual cancer site or type for all women and within certain subgroups. Based on all women, sites for

<table>
<thead>
<tr>
<th>Cancer site or type</th>
<th>All women</th>
<th>Never smokers</th>
<th>Excluding first two years of follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No of cases</td>
<td>Relative risk (95% CI) per 10 unit increase in BMI</td>
<td>No of cases</td>
</tr>
<tr>
<td>Endometrium</td>
<td>2657</td>
<td>2.89 (2.62 to 3.18)</td>
<td>1485</td>
</tr>
<tr>
<td>Adenocarcinoma of oesophagus</td>
<td>150</td>
<td>2.38 (1.59 to 3.56)</td>
<td>53</td>
</tr>
<tr>
<td>Kidney</td>
<td>723</td>
<td>1.53 (1.27 to 1.84)</td>
<td>319</td>
</tr>
<tr>
<td>Leukaemia</td>
<td>635</td>
<td>1.50 (1.23 to 1.83)</td>
<td>318</td>
</tr>
<tr>
<td>Breast (postmenopausal)*</td>
<td>5629</td>
<td>1.40 (1.31 to 1.49)</td>
<td>2855</td>
</tr>
<tr>
<td>Multiple myeloma</td>
<td>491</td>
<td>1.31 (1.04 to 1.65)</td>
<td>253</td>
</tr>
<tr>
<td>Pancreas</td>
<td>795</td>
<td>1.24 (1.03 to 1.48)</td>
<td>305</td>
</tr>
<tr>
<td>Non-Hodgkin's lymphoma</td>
<td>1509</td>
<td>1.17 (1.03 to 1.34)</td>
<td>718</td>
</tr>
<tr>
<td>Ovary</td>
<td>2406</td>
<td>1.14 (1.03 to 1.27)</td>
<td>1256</td>
</tr>
<tr>
<td>Bladder</td>
<td>615</td>
<td>1.09 (0.89 to 1.34)</td>
<td>206</td>
</tr>
<tr>
<td>Cervix</td>
<td>330</td>
<td>1.04 (0.79 to 1.38)</td>
<td>118</td>
</tr>
<tr>
<td>Brain</td>
<td>571</td>
<td>1.01 (0.81 to 1.26)</td>
<td>289</td>
</tr>
<tr>
<td>Colorectum</td>
<td>4008</td>
<td>1.00 (0.92 to 1.08)</td>
<td>1884</td>
</tr>
<tr>
<td>Malignant melanoma</td>
<td>1635</td>
<td>0.94 (0.82 to 1.07)</td>
<td>891</td>
</tr>
<tr>
<td>Stomach</td>
<td>521</td>
<td>0.90 (0.72 to 1.13)</td>
<td>170</td>
</tr>
<tr>
<td>Breast (premenopausal)</td>
<td>1179</td>
<td>0.86 (0.73 to 1.00)</td>
<td>636</td>
</tr>
<tr>
<td>Lung</td>
<td>3171</td>
<td>0.74 (0.67 to 0.82)</td>
<td>269</td>
</tr>
<tr>
<td>Squamous cell carcinoma of oesophagus</td>
<td>263</td>
<td>0.26 (0.18 to 0.38)</td>
<td>83</td>
</tr>
</tbody>
</table>
which we found a significant positive trend in the relative risk of incidence with BMI were endometrial cancer (relative risk per 10 unit increase in BMI = 2.89, 95% confidence interval 2.62 to 3.18), adenocarcinoma of the oesophagus [2.38, 1.59 to 3.56], kidney cancer (1.53, 1.27 to 1.84), leukaemia [1.50, 1.23 to 1.83], post-menopausal breast cancer (1.40, 1.31 to 1.49), multiple myeloma (1.31, 1.04 to 1.65), pancreatic cancer (1.24, 1.03 to 1.48), non-Hodgkin’s lymphoma (1.17, 1.03 to 1.34), and ovarian cancer (1.14, 1.03 to 1.27). The only cancers for which we found a significant inverse association between BMI and cancer incidence were squamous cell carcinoma of the oesophagus (0.26, 0.18 to 0.38) and lung cancer (0.74, 0.67 to 0.82). We also found evidence of a decrease in the risk of pre-menopausal breast cancer with increasing BMI (0.86, 0.73 to 1.00), although this was of borderline statistical significance (P = 0.05). The trend in the risk of all cancers combined associated with a 10 unit increase in BMI was 1.12 (1.09 to 1.14). When we recalculated trend estimates incorporating updated information on BMI from the first re-survey, the results were essentially unchanged.

Most sites that showed a significant association with BMI among women also showed a similar magnitude of association in never smokers, although the trend estimate in never smokers did not always achieve statistical significance. For lung cancer, the trend among never smokers was non-significant (0.82, 0.59 to 1.13) and somewhat attenuated compared with that in all women (0.74, 0.67 to 0.82). For other smoking related cancers (namely, kidney cancer and

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**Table 3 | Relative risk* of cancer mortality for individual cancer sites or types according to body mass index**

<table>
<thead>
<tr>
<th>Site (ICD-10 code)</th>
<th>No of deaths</th>
<th>FAR (95% CI) for cancer mortality in women with body mass index (kg/m²)</th>
<th>Trend (95% CI) per 10 units</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenocarcinoma of oesophagus (C15)</td>
<td>111</td>
<td>1.35 (0.67 to 2.11) (n=20)</td>
<td>2.24 (1.40 to 3.58)</td>
</tr>
<tr>
<td>Squamous cell carcinoma of oesophagus (C15)</td>
<td>182</td>
<td>2.10 (1.66 to 2.65) (n=75)</td>
<td>1.00 (0.74 to 1.35) (n=44)</td>
</tr>
<tr>
<td>Stomach (C16)</td>
<td>403</td>
<td>1.47 (1.19 to 1.81) (n=92)</td>
<td>0.42 (0.24 to 0.73)</td>
</tr>
<tr>
<td>Colorectum (C18-C20)</td>
<td>1548</td>
<td>1.00 (0.90 to 1.13) (n=302)</td>
<td>0.98 (0.89 to 1.09)</td>
</tr>
<tr>
<td>Pancreas (C25)</td>
<td>1130</td>
<td>1.11 (0.97 to 1.27) (n=231)</td>
<td>1.12 (0.91 to 1.15)</td>
</tr>
<tr>
<td>Lung (C34)</td>
<td>3559</td>
<td>1.16 (1.09 to 1.24) (n=922)</td>
<td>0.84 (0.76 to 0.92)</td>
</tr>
<tr>
<td>Malignant melanoma (C43)</td>
<td>151</td>
<td>1.00 (0.69 to 1.44) (n=29)</td>
<td>0.87 (0.56 to 1.13)</td>
</tr>
<tr>
<td>Premenopausal breast (C50)</td>
<td>83</td>
<td>1.07 (0.68 to 1.68) (n=50)</td>
<td>0.91 (0.49 to 1.70)</td>
</tr>
<tr>
<td>Postmenopausal breast (C50)</td>
<td>637</td>
<td>1.11 (0.92 to 1.34) (n=109)</td>
<td>1.49 (1.27 to 1.75)</td>
</tr>
<tr>
<td>Cervix (C53)</td>
<td>109</td>
<td>0.50 (0.30 to 0.86) (n=14)</td>
<td>1.53 (0.95 to 2.47)</td>
</tr>
<tr>
<td>Endometrium (C54)</td>
<td>236</td>
<td>0.81 (0.57 to 1.17) (n=119)</td>
<td>2.46 (1.78 to 3.39)</td>
</tr>
<tr>
<td>Ovary (C56)</td>
<td>1651</td>
<td>0.96 (0.86 to 1.07) (n=320)</td>
<td>2.28 (1.81 to 2.87)</td>
</tr>
<tr>
<td>Kidney (C64)</td>
<td>382</td>
<td>1.01 (0.79 to 1.30) (n=63)</td>
<td>1.71 (1.39 to 2.09)</td>
</tr>
<tr>
<td>Bladder (C67)</td>
<td>186</td>
<td>1.16 (0.84 to 1.60) (n=61)</td>
<td>1.65 (1.28 to 2.13)</td>
</tr>
<tr>
<td>Non-Hodgkin’s lymphoma (C82-C85)</td>
<td>535</td>
<td>0.85 (0.69 to 1.04) (n=92)</td>
<td>1.15 (0.92 to 1.44)</td>
</tr>
<tr>
<td>Multiple myeloma (C90)</td>
<td>284</td>
<td>0.99 (0.74 to 1.32) (n=446)</td>
<td>1.56 (1.15 to 2.10)</td>
</tr>
<tr>
<td>Leukaemia (C91-C95)</td>
<td>428</td>
<td>0.82 (0.64 to 1.04) (n=67)</td>
<td>1.34 (1.05 to 1.71)</td>
</tr>
<tr>
<td>Brain (C71)</td>
<td>645</td>
<td>1.17 (0.98 to 1.40) (n=123)</td>
<td>1.21 (0.98 to 1.49)</td>
</tr>
<tr>
<td>All cancers (C00-C97, excluding C44)</td>
<td>17 203</td>
<td>1.08 (1.05 to 1.12) (n=3577)</td>
<td>1.06 (1.02 to 1.10)</td>
</tr>
</tbody>
</table>

FAR= floating absolute risk; CI=fixed confidence interval.
*Adjusted for age, geographical region, socioeconomic status, reproductive history, smoking status, alcohol intake, physical activity, and, where appropriate, time since menopause and use of hormone replacement therapy.
†ICD-0 morphology codes 8140/3, 8144/3, 8145/3, 8260/3, 8480/3, 8481/3, 8490/3.
‡ICD-0 morphology codes 8070/3, 8071/3, 8072/1, 8074/3.
§Restricted to never users of hormone replacement therapy.

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adenocarcinoma of the oesophagus) and for leukaemia, the trend in risk with increasing body mass index became greater in magnitude after restriction to never smokers. The trend in risk per 10 unit increase in BMI for all cancers combined was also slightly greater in never smokers (1.20, 1.15 to 1.24) than in all women (1.12, 1.09 to 1.14). When we repeated analyses excluding the first two years of follow-up, the trend estimates were not materially altered.

Figure 3 presents the trend estimates in premenopausal women and postmenopausal never users of hormone replacement therapy for cancer sites with more than 50 cases in women who reported being premenopausal at recruitment. We found significant differences in the trend estimates between premenopausal women and postmenopausal never users of hormone replacement therapy for breast cancer (P<0.0001), endometrial cancer (P=0.0001), colorectal cancer (P=0.03), and malignant melanoma (P=0.05). For colorectal cancer and malignant melanoma, we found positive trends in risk with BMI in premenopausal women (relative risk per 10 unit increase 1.61 and 1.62), but we found no evidence of any association in postmenopausal never users of hormone replacement therapy (0.99 and 0.92). By contrast, increased BMI was associated with a decreased risk of breast cancer in premenopausal women (relative risk 0.86) and an increased risk in postmenopausal women (1.40). For endometrial cancer, we found a significant increase in risk with increasing BMI for both groups, but the magnitude of the trend was substantially greater in postmenopausal women than in premenopausal women (relative risk 3.98 compared with 1.77). Thus, in total, we found a significant increase in risk with increasing BMI in 10 out of the 17 specific types of cancer considered, including eight sites in which a positive association existed in all women and two sites in which it was confined to either premenopausal women (colorectal cancer) or postmenopausal women (breast cancer).

Table 4 presents (for postmenopausal women only) the proportions of incident cancers attributable to being overweight or obese, and to being obese, for those cancers that showed a significant increase in risk with increasing BMI. The estimated proportion of all cancers attributable to being overweight or obese among postmenopausal women was 5%. For endometrial cancer and adenocarcinoma of the oesophagus, about a half of cases (51% and 48%) were attributable to being overweight or obese. By comparison, the estimated proportion of cancers attributable to being overweight or obese was between 10% and 20% for multiple myeloma, kidney cancer, leukaemia, and pancreatic cancer and below 10% for all other specific sites or types listed in table 4. Estimates of attributable risk obtained by using unstratified relative risk estimates did not differ materially from those in the table.

**DISCUSSION**

In this analysis of 43,037 incident cancers and 17,203 deaths from cancer among more than 1.2 million women, we found increasing body mass index to be associated with an increased risk of incident and fatal cancer for all cancers combined and for 10 out of the 17 specific sites or types of cancer considered. Although convincing evidence exists of an adverse effect of increased BMI on the risk of several of these cancers, including postmenopausal breast cancer, endometrial cancer, colon cancer, kidney cancer, and adenocarcinoma of the oesophagus, substantially fewer data exist on the effect of BMI on other cancers. Thus, for many cancer sites, the findings presented here constitute important new evidence. Our data also show that menopausal status is a key factor in the relation between BMI and risk of cancer among...
women, not only for those cancers that are known to be hormonally related, such as breast and endometrial cancer, but also for other common cancers not generally thought to be mediated by hormones.

Female reproductive cancers
Among women, hormonally related cancers such as those of the breast and endometrium have been among those most consistently associated with BMI. The relation between BMI and breast cancer is, however, complicated by the fact that BMI has a different effect on breast cancer risk among premenopausal and postmenopausal women. Our data confirm this observation, in that the risk of breast cancer among premenopausal women decreases with increasing BMI whereas the risk increases with BMI among postmenopausal women who have never used hormone replacement therapy. The increase in the risk of breast cancer with increasing BMI among postmenopausal women is likely to be due to increased concentrations of circulating sex hormones, and strong empirical evidence exists to support this, but the opposite relation among premenopausal women is less well understood.

The increased risk of endometrial cancer with increasing adiposity is also thought to be mediated by concentrations of endogenous sex hormones. Although some studies have examined the risk of endometrial cancer separately among premenopausal and postmenopausal women, they have had relatively few cases among premenopausal women and hence little power to detect an interaction. The substantially greater increase in risk with increasing BMI found here for women who reported being postmenopausal as opposed to premenopausal at recruitment is, therefore, a novel finding. Whereas the effect of obesity on postmenopausal endometrial cancer is thought to be due to increased concentrations of unopposed oestrogens, any effect in premenopausal women may be due to progesterone deficiency rather than an excess of oestrogen; the observed differences in the effect of BMI on risk by menopausal status may reflect these different mechanisms.

Few individual studies have reported a significant effect of adiposity on the risk of ovarian cancer, and the small increase in ovarian cancer risk with increasing BMI found here (relative risk per 10 unit increase in BMI=1.14, 95% confidence interval 1.03 to 1.27) is consistent with the conclusions of a review of the published evidence. Some studies have also suggested that the effect of BMI on ovarian cancer risk is greater in premenopausal women than in postmenopausal women. Our findings with respect to BMI and ovarian cancer in premenopausal and postmenopausal women seem to be consistent with this hypothesis, but, as with previous studies, the numbers of cases among premenopausal women are too few to reliably establish a difference. Thus for cancers of the female reproductive organs, in which the relation with BMI might be expected to be mediated by hormones, the effect of BMI on risk seems to differ markedly in premenopausal and postmenopausal women.

Other cancers
Colorectal cancer has been consistently associated with increased adiposity among men. However, results in women have been less consistent; some studies have reported a positive association, some have reported no association, and others have reported greater effects in younger than in older women. The only previous study that looked at the effect of BMI according to menopausal status found relative risks of colon cancer in obese women compared with non-obese women of 1.88 (1.24 to 2.86) for premenopausal women and 0.73 (0.48 to 1.10) for postmenopausal women (P value for heterogeneity=0.01). Our data show no association between BMI and the overall risk of incidence of or mortality from colorectal cancer among women aged 50-64 at recruitment; however, the effect of increasing BMI on risk does seem to differ between premenopausal and postmenopausal women (P value for heterogeneity=0.03), with a significant increase in risk with increasing BMI among premenopausal women (relative risk=1.61, 1.05 to 2.48) but not among postmenopausal women (0.99, 0.88 to 1.12). This apparent interaction between adiposity and menopausal status may explain, at least in part, the variability in published results on the relation between BMI and colorectal cancer among women.

Relatively few studies have reported on the relation between BMI and haematopoietic cancers, and findings have been equivocal regarding BMI in relation to non-Hodgkin’s lymphoma, multiple myeloma, and leukaemia. Our findings show significant trends of increasing risk with increasing BMI for each type of cancer (relative risk of incidence per 10 unit increase=1.17, 1.31, and 1.50). Data on the risk of malignant melanoma in relation to BMI have also been inconsistent; some studies have found no evidence of an association in either men or women, and others have reported an effect in men but not in women. Although we found no overall association between BMI and malignant melanoma, the effect of

Table 4 | Estimated proportion of all cancers, and of cancers of specific sites, attributable to overweight and obesity in postmenopausal women in UK

<table>
<thead>
<tr>
<th>Site or type</th>
<th>Proportion (% of cancers attributable to body mass index (kg/m²)</th>
<th>≥25 (overweight or obese)</th>
<th>≥30 (obese)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endometrial cancer</td>
<td>51</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>Adenocarcinoma of oesophagus</td>
<td>48</td>
<td>35</td>
<td></td>
</tr>
<tr>
<td>Multiple myeloma</td>
<td>18</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Kidney cancer</td>
<td>15</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Leukaemia</td>
<td>16</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Pancreatic cancer</td>
<td>14</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Breast cancer</td>
<td>7</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Non-Hodgkin’s lymphoma</td>
<td>7</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Ovary</td>
<td>4</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>All cancers</td>
<td>5</td>
<td>4</td>
<td></td>
</tr>
</tbody>
</table>

Data on prevalence of exposure among UK women are based on health survey for England 2004, in which 39% of women aged 55-74 had body mass index 25-30 and 31% had body mass index ≥30.
BMI on risk seemed to be greater in premenopausal women than in postmenopausal women (relative risk of incidence per 10 unit increase = 1.62 ± 0.92; P = 0.05).

Previous studies of the risk of adenocarcinoma of the oesophagus and kidney cancer in relation to BMI have consistently reported a material increase in risk with increasing BMI, and our findings provide further support for these associations. Several large cohort studies have also reported an increase in the risk of pancreatic cancer in obese people compared with non-obese people; estimated relative risks among women ranged from about 1.1 to 1.7. Thus the estimated increase in pancreatic cancer risk reported here (relative risk per 10 unit increase in BMI = 1.24, 1.03 to 1.48) is consistent with these published data.

Two sites for which we found a significant inverse relation between BMI and incidence were lung cancer and squamous cell carcinoma of the oesophagus. Similar findings have been reported previously, but these have typically been viewed with caution owing to uncertainty about the extent to which the association between increased risk and low BMI might be due to recent weight loss among people with preclinical disease or residual confounding with smoking or alcohol intake. In our data, the inverse association between BMI and lung cancer was considerably attenuated when we restricted analyses to never smokers; however, the small number of cases of lung cancer among never smokers means that we had insufficient power to exclude an association. By contrast, the substantial inverse association between BMI and squamous cell carcinoma of the oesophagus remained significant after restriction to never smokers (trend in relative risk per 10 unit increase in BMI = 0.32, 0.17 to 0.63), after exclusion of the first two years of follow-up (0.31, 0.20 to 0.48), and after allowance for a possible interaction between smoking status and alcohol intake. Thus, although we cannot rule out the possibility of residual bias in the relation between BMI and squamous cell carcinoma of the oesophagus, the association seems to be remarkably robust.

Strengths and weaknesses

The Million Women Study includes one in four UK women who were aged 50-64 during the period of recruitment, making it the largest ever study of women’s health. Furthermore, the fact that information on exposure is recorded prospectively ensures that findings are not subject to recall bias. To our knowledge, no previous study has examined the role of BMI in both incidence and mortality of cancer within the same cohort, and this is, therefore, another major strength of the study.

As with most large epidemiological studies, BMI in our cohort was based on self reported height and weight, and although self reported BMI has been shown to be a useful measure of adiposity in epidemiological studies, it is likely to be subject to both random and systematic errors. The random component of this measurement error is likely to be small, and indeed adjustment for regression dilution in these analyses had little impact on the dose-response effect. Any systematic error in self reported BMI is likely to stem from a slight over-reporting of height and under-reporting of weight, leading to an underestimate of BMI. However, the degree of underestimation is proportional to the degree of overweight, and a validation study of 2500 UK women of a similar age found not only that both measures yielded similar rankings with respect to BMI, with a correlation coefficient of 0.97, but also that a close numerical agreement existed between self reported BMI and measured BMI.

For many cancers, weight loss often precedes clinical recognition of the disease and, in affected patients, BMI recorded before diagnosis is an underestimate of their usual BMI. This potential bias, termed reverse causality, can give rise to spuriously increased risks at low levels of BMI. Although exclusion of the first two years of follow-up within these data did not materially affect the findings, the relatively short follow-up period precludes exclusion of longer periods; as reverse causality may exert an influence for as long as 10 years after recruitment, this is a limitation of the study. Furthermore, we had no information on whether women had lost weight in the year or so before recruitment and so were unable to exclude women whose BMI at recruitment was not necessarily representative of their usual BMI.

Previous publications have suggested a non-linear relation between BMI and mortality, with an increased risk at very low levels of BMI as well as at high levels. In our data, the numbers of cancers in women with a BMI below 18.5 was extremely small. Furthermore, the relatively short duration of follow-up available here precludes exclusion of the substantial period of follow-up required to minimise the potential effects of reverse causality. Thus, although we cannot yet answer this question reliably within our cohort, we cannot rule out the possibility of an adverse effect on risk of cancer at extremely low BMI.

In the case of smoking related cancers, residual confounding with smoking history is a key potential source of bias. Few studies have had sufficient power to examine risks reliably in people who have never smoked, but a large study of mortality from cancer found evidence of a greater adverse effect of BMI in never smokers compared with all women for oesophageal cancer, pancreatic cancer, and all cancers (relative risks of any cancer in women with BMI ≥ 40 compared with women of normal BMI = 1.88 and 1.62). In general, exclusion of smokers from the analyses presented here did not materially alter the findings, although the dose-response estimates became slightly more marked for adenocarcinoma of the oesophagus, kidney cancer, leukaemia, and all cancers combined (relative risk per 10 unit increase in BMI for all cancers = 1.20 in never smokers compared with 1.12 in all women).

This report focuses on the relation between BMI, measured in middle age, and the short term risk of cancer and death from cancer. It does not consider the role in the development of cancer of other measures of
Increased body mass index is known to increase the risk of adenocarcinoma of the oesophagus, endometrial cancer, kidney cancer, and postmenopausal breast cancer in women. Body mass index has also been associated with the risk of other, rarer, cancers, but the findings are not yet conclusive.

**WHAT THIS STUDY ADDS**

High body mass index in women may increase the risk of multiple myeloma, leukaemia, pancreatic cancer, non-Hodgkin’s lymphoma, and ovarian cancer. Menopausal status seems to affect the relation between body mass index and risk of breast cancer, endometrial cancer, and colorectal cancer. Among postmenopausal women in the UK, 5% of all cancers (about 6000 annually) are attributable to being overweight or obese. Around half of all cases of endometrial cancer and adenocarcinoma of the oesophagus in postmenopausal UK women are attributable to women being overweight or obese.

Body size, such as waist circumference or waist to hip ratio, or indeed measures of BMI at other stages of life such as puberty and young adulthood. Moreover, as some evidence exists to show, for breast cancer at least, that increased BMI at young ages might be associated with a decreased risk in later life, the effects seen here cannot be assumed to apply to BMI measured at other ages.

**Attributable risks**

In these data, the great majority (81%) of cancers occurred in postmenopausal women, and as considerable differences existed in the effect of BMI on the risk of some cancers according to menopausal status, we confined estimates of attributable risk to postmenopausal women. Although reliably calculating corresponding estimates for premenopausal women on the basis of these data is difficult, the proportion of cancers attributable to being overweight in premenopausal UK women is likely to be less than that for postmenopausal women, because breast cancer is the predominant cancer among premenopausal women and an inverse association exists between BMI and breast cancer risk among such women. On the basis of these results, and current estimates of BMI in postmenopausal women in the UK, we estimate that 5% of all cancers among postmenopausal women in the UK are attributable to being overweight or obese (BMI ≥25) and that 4% are attributable to obesity (BMI ≥30). For endometrial cancer and adenocarcinoma of the oesophagus, BMI represents a major modifiable risk factor; as many as about half of all cases of these cancers in postmenopausal women are attributed to being overweight or obese. Overall, these findings imply that 6000 new cancers annually in postmenopausal women in the UK are due to being overweight or obese, of which 4800 are due to obesity.
Detection of prostate cancer in unselected young men: prospective cohort nested within a randomised controlled trial

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ABSTRACT

Objective To investigate the feasibility of testing for prostate cancer and the prevalence and characteristics of the disease in unselected young men.

Design Prospective cohort nested within a randomised controlled trial, with two years of follow-up.

Setting Eight general practices in a UK city.

Participants 1299 unselected men aged 45-49.

Intervention Prostate biopsies for participants with a prostate specific antigen level of 1.5 ng/ml or more and the possibility of randomisation to three treatments for those with localised prostate cancer.

Main outcome measures Uptake of testing for prostate specific antigen; positive predictive value of prostate specific antigen; and prevalence of prostate cancer, TNM disease stage, and histological grade (Gleason score).

Results 442 of 1299 men agreed to be tested for prostate specific antigen; and prevalence of prostate cancer, TNM disease stage, and histological grade (Gleason score).

Detection of prostate cancer in unselected young men: prospective cohort nested within a randomised controlled trial. Three current trials of treatment are based on screen detected populations: the prostate testing for cancer and treatment study (ProtecT), the prostate cancer intervention versus observation trial, and the surveillance therapy against radical treatment trial. An earlier randomised trial with cases of clinically detected prostate cancer showed a survival benefit of surgery compared with watchful waiting, with a median follow-up of 8.2 years. Extrapolation of these results to screen detected cases was, however, problematic because the cases were clinically detected and there was probably a lead time bias before the onset of symptoms of up to nine years. Therefore, in the absence of evidence from ongoing trials many countries (including the United Kingdom) have pragmatically agreed a policy whereby men aged 50 or more may have a test for prostate specific antigen after discussion with their general practitioner of the risks and benefits of testing.

Men younger than 50 are usually offered the test only if they have a family history of the disease or are of black ethnicity. Guidelines from the American National Comprehensive Cancer Network recommend screening for prostate specific antigen in men from age 40, with retesting either annually or at age 45 depending on the initial test value on the basis of findings in two retrospective cohorts that an increased antigen level in the fourth decade increased the risk of prostate cancer. A recently published retrospective cohort study from Sweden reported a 3.7-fold increase in the odds ratio of detecting prostate cancer after 18 years for a 1 ng/ml increase in the prostate specific antigen result. These results were carefully validated because values for prostate specific antigen can decline...
by up to 38% with incorrect processing and frozen storage.14

Few population based studies of testing for prostate specific antigen have been done in men younger than 50. The prevalence of prostate cancer was 2% in a prospective cohort of 681 men aged 40-49 of African-American origin or with a family history of prostate cancer recruited in the United States.15

Prostate cancer was not found in two of the 44 Austrian blood donors with a prostate specific antigen value of at least 4.0 ng/ml who also had a suspicious result on digital rectal examination and a biopsy, but annual testing subsequently revealed six cases (detection rate 1.1%).16 In a population based Austrian study, 28 of the 2054 men tested had a prostate specific antigen value of at least 2.5 ng/ml and three cases of prostate cancer were identified (1.2%).17

In the prostate testing for cancer and treatment study, unselected men aged 50-69 have been invited for a prostate specific antigen test at nine UK centres since June 2001 to evaluate the effectiveness, cost effectiveness, and acceptability of treatments for clinically localised prostate cancer preceded by community based testing for prostate specific antigen.5

Using the same methods we carried out a nested study in men aged 45-49 to investigate the uptake of testing, the prevalence of prostate cancer, and characteristics of the disease.

METHODS

Since 2001 unselected men aged 50-69 and registered in randomly selected primary care centres in nine cities across the United Kingdom have been invited by letter to take part in the prostate testing for cancer and treatment (ProtecT) study. Full details are published elsewhere.518 Using the same methods, between November 2003 and August 2005 we carried out a nested study of men aged 45-49 and registered with eight general practices in Sheffield, in the north of England. The men were invited by letter to attend clinics for enrolment regardless of previous consultations or urological conditions (except those with major comorbidities that precluded enrolment in the trial). Study nurses explained the risks and benefits of testing for prostate specific antigen and provided details of the study. Eligible men who entered the study were tested. Participants had an additional consent form to return within 24 hours to authorise processing of the test. Participants gave written informed consent.

Diagnostic procedures

Participants with a prostate specific antigen value of 1.5 ng/ml or more were invited for a transrectal ultrasound guided systematic prostate biopsy involving 10 core specimens, a repeat prostate specific antigen test, and a digital rectal examination. We selected a prostate specific antigen threshold for biopsy of 1.5 ng/ml to optimise detection of prostate cancer while reducing the number of unnecessary biopsies, on the basis of data from a Swedish cohort of younger men.14 A second biopsy was offered to those with either high grade prostatic intraepithelial neoplasia, atypical small acinar proliferation, a negative biopsy result but a persistently raised prostate specific antigen level, or a palpable abnormality on digital rectal examination. In addition, we offered annual tests to those men with a negative biopsy result. Men with an initial prostate specific antigen value of less than 1.5 ng/ml were not further tested. Participants with clinically localised prostate cancer were eligible for randomisation to radical three dimensional conformal radiotherapy, radical prostatectomy, or active monitoring (regular tests for prostate specific antigen and disease monitoring), with follow-up every 3-6 months for all arms according to treatment and study research protocols (mean follow-up 24 months).

Outcome assessment and statistical analysis

Research nurses recorded clinical and trial details on study databases. At enrolment, data were collected on participants’ sociodemographic characteristics, including previous test results for prostate specific antigen that were checked against medical records. Ethnicity was based on categories from the 1991 UK census. Specialist uropathologists reported the biopsy and disease results. We classified the results of digital rectal examinations as positive if there was a palpable abnormality. Tumours were assessed by histological grading using the Gleason scoring system (6-10); tumour staging using the 2002 TNM classification; and a nomogram for predicting indolent disease in men aged 50 or more.19 We calculated the positive predictive value of the prostate specific antigen test,
with the biopsy as the reference test. All analyses were done using Stata version 9.

RESULTS
Overall, 524 of 1299 unselected men (40%) aged 45-49 invited attended a study enrolment clinic; 473 (36.4%) were included in the study (fig 1). Thirty two chose not to be tested (2%) and 19 (1%) were excluded for other reasons: 16 were medically unsuitable for the cancer treatments, two could not give informed consent, and one was outside the age range. Four hundred and forty two participants (34%) gave additional consent to process their prostate specific antigen test.

The mean age of participants was 48 years and 413 were white (98%). Ten of the participants had prostate cancer. These participants were white and did not report a family history of the disease compared with 22 of 422 (5%) participants without cancer. None of the 18 participants who had been previously tested for prostate specific antigen (4%) had a diagnosis of prostate cancer. Three hundred and fifty three participants (97%) reported that urinary symptoms had little or no effect on their life.

Detection of prostate cancer
The mean value for prostate specific antigen was 0.9 (SD 0.75) ng/ml and the median was 0.7 ng/ml (fig 2). Fifty four participants had raised levels of prostate specific antigen (12.2% of those enrolled) and 47 underwent a biopsy (87%): four declined, two were unfit for the procedure, and results for one who had a biopsy elsewhere were unavailable. Twelve participants had repeat biopsies after consultation with the urologist and two after findings of high grade prostatic intraepithelial neoplasia. In those men who did not have a further biopsy after an initial negative biopsy result, 10 were referred back to their general practitioners, five declined a biopsy, one had an unavailable result, and eight elected to undergo further testing at 12 months.

Nine cases of prostate cancer were detected at the first biopsy and one at the second and all the initial values for prostate specific antigens were less than 4.0 ng/ml. The detection rate for prostate cancer was 2.3% and the prevalence of disease in participants with a raised level of prostate specific antigen was 21.3% (95% confidence interval 7.4% to 29.6%). The positive predictive value of the prostate specific antigen test was 21.3% (25.6% when corrected for participants who did not undergo a biopsy).

Clinical and disease features of the cancers
Eight participants had two or more positive biopsy core results and five had four or more positive results. The total tumour length ranged from less than 0.5 mm to 24 mm, with a maximum of 13 mm in a single core (table). Perineural invasion was reported in three cases. Nine participants had cT1c tumours, Gleason score 6, of whom eight had a negative digital rectal examination result (one result was unavailable). One participant had a cT2c tumour, Gleason score 7 (3+4), and a positive digital rectal examination result. Five cases were classified as potentially indolent using a nomogram and five were classified as of potential clinical significance.19

Five participants agreed to be randomised (55%); one to active monitoring and two each to radiotherapy and surgery. One participant randomised to surgery rejected the allocation and selected radiotherapy. Two participants chose active monitoring, one radiotherapy, one brachytherapy. The comorbidities of one participant precluded randomisation and he received radiotherapy. Disease stage was organ confined with no evidence of nodal metastases (pT2aN0Mx) for the participant who received a radical prostatectomy, with a Gleason score of 6 (3+3). The surgical margins were negative with no evidence of

<table>
<thead>
<tr>
<th>Case No</th>
<th>Initial result</th>
<th>Second result</th>
<th>Digital rectal examination result</th>
<th>TNM stage</th>
<th>Gleason score*</th>
<th>Biopsy positive cores†</th>
<th>Total tumour length (mm)</th>
<th>Perineural invasion</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2.5</td>
<td>0.3</td>
<td>Positive</td>
<td>cT2c</td>
<td>7</td>
<td>5</td>
<td>22</td>
<td>Yes</td>
</tr>
<tr>
<td>2</td>
<td>2.0</td>
<td>3.0</td>
<td>Negative</td>
<td>cT1c</td>
<td>6</td>
<td>5</td>
<td>24</td>
<td>Yes</td>
</tr>
<tr>
<td>3</td>
<td>1.7</td>
<td>1.3</td>
<td>Negative</td>
<td>cT1c</td>
<td>6</td>
<td>4</td>
<td>10</td>
<td>No</td>
</tr>
<tr>
<td>4</td>
<td>3.5</td>
<td>2.8</td>
<td>Negative</td>
<td>cT1c</td>
<td>6</td>
<td>4</td>
<td>8</td>
<td>No</td>
</tr>
<tr>
<td>5</td>
<td>3.8</td>
<td>3.3</td>
<td>Negative</td>
<td>cT1c</td>
<td>6</td>
<td>4</td>
<td>4</td>
<td>No</td>
</tr>
<tr>
<td>6</td>
<td>1.6</td>
<td>2.0</td>
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<td>2</td>
<td>6</td>
<td>No</td>
</tr>
<tr>
<td>7</td>
<td>1.7</td>
<td>1.6</td>
<td>NA</td>
<td>cT1c</td>
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<td>2</td>
<td>4</td>
<td>No</td>
</tr>
<tr>
<td>8</td>
<td>1.9</td>
<td>1.8</td>
<td>Negative</td>
<td>cT1c</td>
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<td>2</td>
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</tr>
<tr>
<td>9</td>
<td>1.8</td>
<td>1.3</td>
<td>Negative</td>
<td>cT1c</td>
<td>6</td>
<td>1</td>
<td>3</td>
<td>Yes</td>
</tr>
<tr>
<td>10</td>
<td>1.6</td>
<td>1.4</td>
<td>Negative</td>
<td>cT1c</td>
<td>6</td>
<td>1</td>
<td>&lt;0.5</td>
<td>No</td>
</tr>
</tbody>
</table>

cT2c=tumour palpable in both lobes on digital rectal examination; cT1c=non-palpable tumour found in needle biopsies carried out because of raised prostate specific antigen levels. NA=not available.
*6=somewhat resembling normal tissue, 7=barely normal tissue, mostly low grade but with some high grade areas.
†10 cores were taken from each participant.
extracapsular or perineural spread of the disease. No biochemical failure in the form of a rising prostate specific antigen was detected in nine of the 10 cases over a mean of 24 months’ follow-up (one participant was lost to follow-up).

**DISCUSSION**

The uptake of prostate specific antigen testing within the context of a clinical trial in unselected men aged 45-49 was 34% and the prevalence of prostate cancer was 2.3%, with five of the 10 cancers classified as potentially clinically significant.

Men aged 45-49 had a significantly lower uptake of testing (34.0%, 95% confidence interval 31.2% to 36.3%) compared with those aged 50-69 (50%, 49.7% to 50.3%) in the main prostate testing for cancer and treatment study. The uptake of testing was 25%-46% in the European randomised screening for prostate cancer trial with older participants and 32% in an Austrian study with younger men. The American high risk cohort of younger men was recruited by using a press release so the response rate is unknown.

The detection rate for prostate cancer in the prostate testing for cancer and treatment study was broadly similar in younger (2.3%, 0.9% to 3.7%) and older men (2.9%, 2.7% to 3.0%). If all participants had been offered biopsies using the same prostate specific antigen threshold, however, a greater difference may have emerged, as the threshold for the older men was 3.0 ng/ml but prostate specific antigen values between 2.0 and 3.0 ng/ml are also associated with a slightly increased risk of prostate cancer. The prevalence of prostate cancer reported here was higher than the Austrian studies in younger men and comparable to the American high risk cohort. However, we used systematic 10 core biopsies (adding two lateral biopsies on each side) in this study, which are more optimal for cancer detection than the previously used sextant biopsy scheme (three biopsies from each side including base, middle, and apex of the prostate). Data on prevalence were also less accurate in previous cohort studies as only about 50% of men with a raised prostate specific antigen level had a biopsy. It is also noteworthy that those men with the highest values for prostate specific antigen were not found to have cancer (fig 2 and table), confirming the low specificity of the test.

The prognosis of prostate cancers detected by screening is a critical problem with results from the European randomised screening for prostate cancer trial indicating that about half of the cancers detected are clinically indolent. Half the cancers were categorised as potentially indolent in our study, although the nomogram used in the European trial has yet to be validated in this age range. All cases were clinically localised in the younger men compared with 76% in men aged 50-69 in the prostate testing for cancer and treatment study, but more accurate assessment of disease data was not possible in those receiving non-surgical treatments. The 26 cancers detected in the American study were clinically localised, with a mean Gleason score of 6, whereas disease staging showed that 18 of 24 cases (78%) were localised tumours, with a mean Gleason score of 6. Biochemical disease progression in the form of a rising prostate specific antigen occurred in six cases (24%) over two years’ follow-up, but this short period did not permit comparison of outcome between younger and older men. In the smaller Austrian study, five detected tumours were localised and Gleason scores ranged from 4-8. None of the prospective cohorts of younger men yet has sufficient follow-up to inform the debate on the long term outcome of these cancers detected by testing for prostate specific antigen. In the only outcome data published in men younger than 50, survival without biochemical relapse (in the form of rising prostate specific antigen) after radical prostatectomy seemed better in younger men.

Our study has several strengths but also some limitations. The major strength is the prospective design using an unselected population with minimal contamination of the prevalence data by previous testing for prostate specific antigen, which is not routinely recommended in the United Kingdom. Study results were also enhanced by the high uptake for biopsy, the use of a systematic 10 core biopsy protocol, detailed histology, and standardised diagnosis algorithms.

The limitations were that testing was done within the context of a clinical trial, which, along with trial exclusion criteria, probably reduced uptake. Enrolment in clinical trials is higher in older age groups probably because of the perceived additional demands of time and visits to the research centre. Although the study was population based there may have been self selection criteria by participants who may have attended because of minor health problems, general anxiety, or misconceptions about the disease and its implications, but these were not related to urinary symptoms, which were infrequently reported. It is not possible to examine the characteristics of the non-responders because of the UK Data Protection Act 1998. The study population was predominately white (reflecting the population of the catchment’s
One in two cancers detected is potentially clinically important but the prognosis is currently unknown.

The uptake of testing for prostate specific antigen by men aged 45-49 was 34% and the prevalence of prostate cancer was 2.3%. Younger men were less likely to subscribe to testing than those older than 49. One in two cancers detected is potentially clinically important but the prognosis is currently unknown.

WHAT IS ALREADY KNOWN ON THIS TOPIC
Screening for prostate cancer, when undertaken, usually starts at age 50, in the absence of risk features. A lower age limit has recently been adopted in the United States on the basis of two retrospective cohorts, which found that prostate specific antigen levels in the fourth decade predicted prostate cancer.

WHAT THIS STUDY ADDS
The uptake of testing for prostate specific antigen by men aged 45-49 was 34% and the prevalence of prostate cancer was 2.3%. Younger men were less likely to subscribe to testing than those older than 49. One in two cancers detected is potentially clinically important but the prognosis is currently unknown.

Potential benefits and harms of prostate cancer testing
This study provides evidence to inform the debate about testing and screening for prostate cancer in men aged less than 50. Firstly, it has shown that men invited to testing will attend, but at a much lower rate than older men, and so if screening was introduced greater efforts would have to be made to maximise uptake in this age group. Secondly, it has confirmed that a prostate specific antigen threshold of 1.5 ng/ml results in a comparable detection rate to that in older men with a threshold of 3.0 ng/ml. At present, however, it is not possible to determine which tumours would result in clinically significant disease and which represent indolent disease.

One study advocated that screening for prostate cancer should start at age 45. If the 2,236,000 men aged 45-49 in the UK population (UK Office of National Statistics, 2004) were to undergo screening for prostate specific antigen it can be projected from our data that 272,905 men would have raised a prostate specific antigen level and, of these, 51,499 would have prostate cancer. Some of these cancers may benefit from treatment although this has to be set against the possible distress caused to the 221,456 men with negative biopsy results, and the risks of overtreatment and associated side effects to those with a diagnosis of cancer.

Some of these issues may be resolved by the development of robust prognostic nomograms and biomarkers to reliably identify clinically significant disease. Furthermore, randomised trials currently under way should resolve the controversies around the testing for and treatment of prostate cancer. This study will inform the debate about thresholds for prostate specific antigen and age limits only if screening for prostate cancer is proved to be effective in these ongoing trials.

We thank the research group of the prostate testing for cancer and treatment study for their contribution and Richard Martin for his comments.

Contributors: JAL, JLD, DEN, and FCH had full access to the data in the study. JAL is the trial coordinator. JLD, DEN, and FCH are the principal investigators. JH, JRG, and FCH carried out the substudy. DJD, LD, and ELT contributed to data collection and analysis. JAL wrote the first draft and together with FCH wrote the final manuscript. All authors contributed to the intellectual content of the draft manuscript and approved the final version. JAL is guarantor of the paper.

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Public information needs after the poisoning of Alexander Litvinenko with polonium-210 in London: cross sectional telephone survey and qualitative analysis

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ABSTRACT

Objectives To identify public perceptions of the risk to health after the poisoning of Alexander Litvinenko with polonium-210 (210Po) in London and to assess the impact of public health communications.

Design Cross sectional telephone survey and qualitative interviews.

Setting London, United Kingdom.

Participants 1000 people completed the cross sectional survey and 86 potentially exposed people completed the qualitative interviews.

Main outcome measures Perception of risk to personal health after the 210Po incident. Qualitative interviews were analysed with an emphasis on information needs.

Results 11.7% of the survey sample (n=117) perceived their health to be at risk. Aside from personal variables the main predictors of perceived risk to health were believing that the incident was related to terrorism (odds ratio 2.7, 95% confidence interval 1.5 to 4.6) rather than to espionage, that it was targeted at the wider public rather than one person (5.9, 3.2 to 10.9), and that it could affect people who had not been in the contaminated area (3.2, 2.1 to 5.1). Participants in the qualitative interviews were generally satisfied with the information they had received, although they would have preferred more information about their individual risk of exposure, the results of their urine tests, and the health implications of the incident.

Conclusions Perceptions of the public that the 210Po incident in London in 2006 was related to espionage helped to reassure them that the risks to personal health were low. In the event of future incidents it is important to ensure that detailed, comprehensible information about the risks of any exposure is available.

INTRODUCTION

People’s subjective assessment of the risk posed by exposure to harmful substances in the environment can show a noticeable discrepancy with the objective level of risk involved. Certain scenarios tend to be associated with increased perceptions of risk, with substances that are manmade, have dreaded consequences, involve involuntary exposure, are hard to detect, or cause disagreement among experts all tending to lead to greater concern.1,2 Given that increased perceptions of risk can in turn lead to increased anxiety and behavioural changes,3 how the public perceives a hazard can play an important part in determining its medical, social, and economic effects.

During major incidents that impact on public health, health agencies and emergency services often need to reassure the public about the level of risk involved, advise about measures being taken to safeguard their health, and specify what personal actions can be taken to minimise risk.1,2,4 This communication can be challenging. In the face of scientific uncertainties, changing situations, constant requests from the media for information, and staff under intense pressure, it can be hard to provide timely, clear, and consistent information.5 Knowing what the public already understand about an incident or health hazard can help, by alerting communicators to any unfounded fears of the public and allowing them to ensure that their messages resonate with pre-existing beliefs.1 Identifying these beliefs before an incident can be even more helpful, as this allows appropriate messages to be developed and tested and then used quickly in emergencies.6 Although studies on patient information needs relating to chemotherapy or radiotherapy exist,7 it is difficult to extrapolate from therapeutic approaches to unexpected exposures that produce no beneficial effect. As there have been few incidents involving the intentional release of radiological agents, previous studies that have assessed risk perceptions relating to these scenarios have relied mainly on focus groups, interviews, or simulations to produce evidence about what risk communication strategies might be helpful. Despite these studies providing valuable insights they can never replicate the sensations of threat during a real incident. Learning lessons from events in the real world is therefore vital.

We assessed the public’s perceptions of risk to the release of polonium-210 (210Po) in central London in...
November 2006, when Alexander Litvinenko was poisoned. We also assessed the public’s knowledge and perceptions of the communication strategies used at that time by the UK’s Health Protection Agency, the body responsible for protecting public health during the incident. As perceptions of an incident probably differ depending on someone’s involvement, we used two approaches in this study: a cross sectional telephone survey of a representative sample of adult Londoners and in-depth qualitative interviews with people who had been in two areas known to have been contaminated during the incident. In our survey we tested whether knowledge about $^{210}$Po or perceptions of the nature of the incident were associated with a reduced perception of risk. In our qualitative interviews we assessed what incident specific or communication factors were associated with increased anxiety among potentially exposed people and whether any deficits could be identified in the information provided by the Health Protection Agency.

**METHODS**

After the death of Alexander Litvinenko on 23 November 2006 from $^{210}$Po poisoning, the Health Protection Agency started a public health response to assess risk to people potentially exposed to this radioactive isotope and to offer them a test. Investigations initially centred on a sushi restaurant in central London and the bar of a London hotel. The public were advised to telephone NHS Direct if they had been in either venue on 1 November and were asked about symptoms of acute $^{210}$Po poisoning. When requested by callers, clinical staff at the Health Protection Agency returned phone calls, assessed people further, and offered a urine test for $^{210}$Po if indicated. On 7 December this protocol changed after several members of the hotel’s staff tested positive for $^{210}$Po: people were now asked to contact the Health Protection Agency if they had been in the hotel bar between 31 October and 2 November, and were offered a urine test. People who had contacted the agency before 7 December were advised about the changed risk assessment by letter. Throughout this period the media focused on rumours of an espionage involvement, while the Health Protection Agency produced almost daily press releases and briefings tackling the resulting public health issues.

**Cross sectional telephone survey**

Between 8 and 11 December 2006 Ipsos MORI carried out a telephone survey of 1000 adult Londoners, using random digit dialling. Proportional quota sampling ensured that respondents were demographically representative of the general London population, with quotas based on sex, age, employment status, residential location, home ownership, and ethnicity. The primary outcome was whether participants perceived that their own health was at risk as a result of the $^{210}$Po incident. Perceiving personal health to be at risk was defined as a response of 3 or 4 to the question: “On a scale of 0 to 4, where 0 is not at all and 4 is a lot, to what degree do you feel your health is at risk as a consequence of the recent radiation incidents?” Predictor variables consisted of personal details; how well informed participants believed they were about the radiation incidents; accuracy on nine true or false items relating to $^{210}$Po, whether participants believed the incident was best described as terrorism, a public health threat, a crime, espionage or spying; whether participants believed the incident was intended to harm only one person, a small number of specific people, or the wider public; and whether participants believed that the advice to contact NHS Direct was an under-reaction, over-reaction, or about right. Eight of the nine true or false items reflected information conveyed in press releases issued by the Health Protection Agency in the period immediately before our survey. A ninth item, concerning the lack of a treatment for $^{210}$Po poisoning, was not explicitly included in these releases. Each interview lasted 15 to 20 minutes.

**Qualitative sampling**

Participants from four groups were selected for our qualitative interviews. The first consisted of people who had been in the sushi restaurant on 1 November, had contacted NHS Direct, and had given permission for the Health Protection Agency to contact them. The other three groups consisted of people who had been in the hotel bar between 31 October and 2 November and who had either accepted the offer of urine testing, refused this offer, or failed to reply to the Health Protection Agency after being informed about their eligibility for urine testing.

Potential participants were sent letters explaining that researchers would be in touch to find out about their views and experiences. As long as an opt-out was not received, participants were telephoned and an interview completed. Interviewers were provided with scripts to ensure that each participant was asked the same questions but were also instructed to probe for further detail in areas that seemed important to the respondent. For the restaurant sample, interviews focused on reasons for contacting NHS Direct, how participants would describe the $^{210}$Po incident, what information was received from NHS Direct or the Health Protection Agency, how helpful or reassuring that was, and what effects the incident had had on their lives. Although these participants were not routinely offered urine testing, we asked them whether they would have accepted a test if it had been offered, and why. Interviews with participants from the hotel groups were similar but also included questions about why they had accepted or declined urine testing, what their understanding of the results were, and whether they would have liked more information about any aspect of the test. In addition, participants were asked to rate how much they thought their health was at risk immediately before contacting NHS Direct, using the same item as used in our cross sectional survey.

Participants from the restaurant sample were interviewed between 27 December 2006 and 5 January 2007. Those from the hotel samples were interviewed between 22 January and 8 February 2007. Within each
group, potential participants were selected at random from records kept by the Health Protection Agency until we thought that no new information was being learnt from the interviews.

Analyses
We weighted the survey data to ensure that the groups were representative of the London population. We calculated odds ratios for the association between each personal variable and perceived risk to health as a result of the incident. We used being Muslim as the reference category for religion given a previously identified association between being Muslim and experiencing heightened distress after the London bombings on 7 July 2005. To assess whether perceptions of, or knowledge about, the incident had any impact on risk perceptions over any effects of the personal variables, we calculated odds ratios for non-personal predictors using separate binomial logistic regressions adjusting for sex, age, income, ethnicity, and religion. These potential confounders were chosen a priori as variables likely to have an impact on risk perception. We used SPSS version 12.0.1 for statistical analyses.

GJR and LP coded the transcripts of interviews using techniques adapted from grounded theory methods. Statements within each interview were first grouped into categories, using headings that seemed to reflect the overarching theme being discussed. After the main categories had been defined by the coders, variables within each category were identified by grouping statements together that reflected the same core issue (for example, “anxiety” or “family pressure” as variables within the category “reasons for calling NHS Direct”).

RESULTS
Of the 11 058 eligible respondents contacted for the cross sectional survey, 1238 agreed to participate and

<table>
<thead>
<tr>
<th>Variables</th>
<th>No (%)</th>
<th>No (%) perceiving health at risk</th>
<th>Unadjusted odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td>510 (51)</td>
<td>73 (14)</td>
<td>1.7 (1.2 to 2.6)</td>
</tr>
<tr>
<td>Men</td>
<td>490 (49)</td>
<td>44 (9)</td>
<td>Reference</td>
</tr>
<tr>
<td>Age (years):</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-24</td>
<td>124 (12)</td>
<td>15 (12)</td>
<td>1.6 (0.7 to 3.4)</td>
</tr>
<tr>
<td>25-34</td>
<td>251 (25)</td>
<td>33 (13)</td>
<td>1.7 (0.9 to 3.4)</td>
</tr>
<tr>
<td>35-54</td>
<td>361 (36)</td>
<td>42 (12)</td>
<td>1.5 (0.8 to 2.8)</td>
</tr>
<tr>
<td>55-64</td>
<td>111 (11)</td>
<td>14 (13)</td>
<td>1.6 (0.7 to 3.6)</td>
</tr>
<tr>
<td>≥64</td>
<td>153 (15)</td>
<td>13 (9)</td>
<td>Reference</td>
</tr>
<tr>
<td>Ethnicity:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-white</td>
<td>289 (29)</td>
<td>58 (20)</td>
<td>2.8 (1.9 to 4.1)</td>
</tr>
<tr>
<td>White</td>
<td>711 (71)</td>
<td>59 (8)</td>
<td>Reference</td>
</tr>
<tr>
<td>Religion:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>294 (29)</td>
<td>19 (7)</td>
<td>0.2 (0.1 to 0.4)</td>
</tr>
<tr>
<td>Other faith</td>
<td>637 (64)</td>
<td>80 (13)</td>
<td>0.4 (0.2 to 0.7)</td>
</tr>
<tr>
<td>Muslim</td>
<td>69 (7)</td>
<td>18 (26)</td>
<td>Reference</td>
</tr>
<tr>
<td>Yearly income (n=842):</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;£30 000</td>
<td>487 (58)</td>
<td>86 (18)</td>
<td>4.6 (2.6 to 7.9)</td>
</tr>
<tr>
<td>≥£30 000</td>
<td>355 (42)</td>
<td>16 (5)</td>
<td>Reference</td>
</tr>
<tr>
<td>Parental status:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Children under 18</td>
<td>316 (32)</td>
<td>38 (12)</td>
<td>1.0 (0.7 to 1.6)</td>
</tr>
<tr>
<td>No children</td>
<td>684 (68)</td>
<td>79 (12)</td>
<td>Reference</td>
</tr>
<tr>
<td>Pregnancy status:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Self or partner is pregnant</td>
<td>36 (4)</td>
<td>6 (17)</td>
<td>1.6 (0.7 to 3.9)</td>
</tr>
<tr>
<td>Neither self nor partner pregnant</td>
<td>964 (96)</td>
<td>110 (11)</td>
<td>Reference</td>
</tr>
<tr>
<td>Working status:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Working full or part time</td>
<td>622 (62)</td>
<td>68 (11)</td>
<td>0.8 (0.6 to 1.3)</td>
</tr>
<tr>
<td>Not working</td>
<td>378 (38)</td>
<td>48 (13)</td>
<td>Reference</td>
</tr>
<tr>
<td>Housing tenure:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rented</td>
<td>395 (40)</td>
<td>60 (15)</td>
<td>1.7 (1.2 to 2.5)</td>
</tr>
<tr>
<td>Owner</td>
<td>605 (61)</td>
<td>57 (9)</td>
<td>Reference</td>
</tr>
<tr>
<td>Frequency of travel to central London:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than weekly</td>
<td>497 (50)</td>
<td>69 (14)</td>
<td>1.5 (1.0 to 2.3)</td>
</tr>
<tr>
<td>Once a week or more</td>
<td>503 (50)</td>
<td>48 (10)</td>
<td>Reference</td>
</tr>
</tbody>
</table>

Total sample size for each variable is 1000, unless stated otherwise. Samples of fewer than 1000 result from refusals, “don’t know,” or “other” responses.
1000 completed interviews (9.1%). Overall, 117 of these respondents (11.7%) were categorised as perceiving their health to be at risk as a result of the $^{210}$Po incident during which Alexander Litvinenko was poisoned (table 1). Levels of knowledge about $^{210}$Po were generally low, with recognition of messages from the Health Protection Agency ranging from 15% (if $^{210}$Po gets on to your clothes it can be removed using a normal washing machine) to 58% ($^{210}$Po is usually dangerous only if it enters your body; table 2). The exception was for the statement that “If you have not been in one of the areas known to be contaminated with $^{210}$Po, then there is no risk to your health”: 71% of the sample recognised that this was correct. Regarding perceptions of the event (table 3), most participants believed that the incident was related to a crime or to espionage (68%) and that it was not targeted at the wider public (86%). Most also thought the Health Protection Agency’s response to the incident had been appropriate or about right (80%).

**Personal variables associated with risk perception**

Unadjusted odds ratios showed that being female (1.7, 95% confidence interval 1.2 to 2.6), being of non-white ethnicity (2.8, 1.9 to 4.1), having a household income of less than £30 000 (€43 000; $61 000) yearly (4.6, 2.6 to 7.9), being in rented accommodation (1.7, 1.2 to 2.5), and travelling into central London less than once a week (1.5, 1.0 to 2.3) were associated with perceiving personal health to be at risk. Subscribing to no religion (0.2, 0.1 to 0.4) or any other religion (0.4, 0.2 to 0.7) was associated with a lower likelihood of perceived risk to health than being Muslim (table 1).

---

**Table 2** Knowledge related predictors of perception that personal health is at risk after incident in which Alexander Litvinenko was poisoned with polonium-210 ($^{210}$Po) in London

<table>
<thead>
<tr>
<th>Variables</th>
<th>No (%)</th>
<th>No (%) perceiving health at risk</th>
<th>Unadjusted odds ratio (95% CI)</th>
<th>Adjusted odds ratio (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>How well informed do you think you are about health risks relating to the recent radiation incidents? (<em>n</em>=987):</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not well informed (0 or 1)†</td>
<td>372 (38)</td>
<td>52 (14)</td>
<td>1.4 (0.9 to 2.0)</td>
<td>1.0 (0.7 to 1.6)</td>
</tr>
<tr>
<td>Well informed (2-4)</td>
<td>614 (62)</td>
<td>64 (10)</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>$^{210}$Po occurs naturally in the environment [true]:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incorrect or don’t know</td>
<td>726 (73)</td>
<td>87 (12)</td>
<td>1.1 (0.7 to 1.8)</td>
<td>1.3 (0.8 to 2.1)</td>
</tr>
<tr>
<td>Correct</td>
<td>274 (27)</td>
<td>29 (11)</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Exposure to $^{210}$Po is always fatal [false]:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incorrect or don’t know</td>
<td>424 (42)</td>
<td>72 (17)</td>
<td>2.5 (1.6 to 3.6)</td>
<td>1.6 (0.9 to 2.3)</td>
</tr>
<tr>
<td>Correct</td>
<td>576 (58)</td>
<td>45 (8)</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>$^{210}$Po is usually dangerous only if it enters your body—for example, if you eat it [true]:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incorrect or don’t know</td>
<td>416 (42)</td>
<td>68 (16)</td>
<td>2.1 (1.4 to 3.1)</td>
<td>1.6 (1.0 to 2.5)</td>
</tr>
<tr>
<td>Correct</td>
<td>584 (58)</td>
<td>49 (8)</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>If $^{210}$Po gets on to your clothes it can be removed using a normal washing machine [true]:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incorrect or don’t know</td>
<td>852 (85)</td>
<td>105 (12)</td>
<td>1.7 (0.9 to 3.1)</td>
<td>1.3 (0.7 to 2.6)</td>
</tr>
<tr>
<td>Correct</td>
<td>148 (15)</td>
<td>12 (8)</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Most people exposed to $^{210}$Po start to feel ill within a few days [false]:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incorrect or don’t know</td>
<td>739 (74)</td>
<td>98 (13)</td>
<td>2.0 (1.2 to 3.4)</td>
<td>1.7 (0.9 to 3.0)</td>
</tr>
<tr>
<td>Correct</td>
<td>261 (26)</td>
<td>19 (7)</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>The main health effects of $^{210}$Po can take years to develop [true]:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incorrect or don’t know</td>
<td>610 (61)</td>
<td>76 (13)</td>
<td>1.2 (0.8 to 1.8)</td>
<td>1.1 (0.7 to 1.8)</td>
</tr>
<tr>
<td>Correct</td>
<td>390 (39)</td>
<td>41 (11)</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>It takes only a few minutes for scientists to test if you have been exposed to $^{210}$Po [false]:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incorrect or don’t know</td>
<td>631 (63)</td>
<td>76 (12)</td>
<td>1.1 (0.7 to 1.7)</td>
<td>1.3 (0.8 to 2.1)</td>
</tr>
<tr>
<td>Correct</td>
<td>369 (37)</td>
<td>41 (11)</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Medicines are available that can prevent people exposed to $^{210}$Po from becoming ill [false]:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incorrect or don’t know</td>
<td>415 (42)</td>
<td>55 (13)</td>
<td>1.3 (0.9 to 1.9)</td>
<td>1.1 (0.7 to 1.6)</td>
</tr>
<tr>
<td>Correct</td>
<td>585 (59)</td>
<td>62 (11)</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>If you have not been in one of the areas known to be contaminated with $^{210}$Po then there is no risk to your health [true]:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incorrect or don’t know</td>
<td>292 (29)</td>
<td>67 (23)</td>
<td>3.9 (2.6 to 5.8)</td>
<td>3.2 (2.1 to 5.1)</td>
</tr>
<tr>
<td>Correct</td>
<td>708 (71)</td>
<td>50 (7)</td>
<td>Reference</td>
<td>Reference</td>
</tr>
</tbody>
</table>

*Adjusted for sex, age, income, ethnicity, and religion.
†Scale from 0 (not at all) to 4 (a lot).
Knowledge or perceptions of the incident and risk perception

Odds ratios adjusted for age, sex, income, ethnicity, and religion showed that believing that 210Po can be dangerous even if it does not enter the body (1.6, 1.0 to 2.5) and believing that 210Po can pose a risk to people who have not entered a contaminated area (3.2, 2.1 to 5.1) were associated with increased perceptions of risk to personal health (table 2). Participants who believed that the incident was related to terrorism (2.7, 1.5 to 4.6) or was a threat to public health (1.9, 1.1 to 3.4) were more likely to believe that their own health was at risk than those who reported that it was related to crime or espionage (table 3). Participants who thought that the incident was aimed at the wider public were more likely to perceive that their own health was at risk than those who believed that it was targeted at only one person (5.9, 3.2 to 10.9).

Qualitative results

Sixteen women and 15 men (mean age 35 [SD 10] years) were interviewed for the restaurant sample. Twenty two did not participate: three who had not been in the restaurant, five who declined to participate, and 14 who could not be contacted. For the hotel samples, 37 men and 18 women (mean age 43 [SD 12] years) were interviewed, including 24 people who accepted a urine test, 21 who failed to respond to the Health Protection Agency’s letter, and 10 who declined testing. Non-responders consisted of nine people who had not been in the hotel on a relevant date, one who was aged less than 18 years, three who declined to participate, and 27 who could not be contacted. Of the 78 participants who answered the question on income, 65 (83%) had annual household incomes of over £30 000. Two of 31 (6%) participants from the restaurant sample reported believing that their health was at risk before contacting NHS Direct, compared with 7 of 53 (13%) participants from the hotel sample.

Reasons for calling NHS Direct

Four motivating factors given for contacting NHS Direct were pressure from friends or relatives, official guidance, civic duty, and anxiety.

Descriptions of the incident

When participants were asked to describe recent events their responses reflected four main themes. Exotic descriptions emphasised the unusual or bizarre nature of the incident—for example, “It seems like it is in the wrong place. It doesn’t seem like it should be happening in London.” Menacing descriptions, which were relatively rare, included comments such as “it is quite shocking,” or “quite sinister.” More common were descriptions comparing events to a spy story, with James Bond being mentioned several times. The precise targeting of the incident was mentioned by several participants.

Initial sources of anxiety

Several factors affected initial levels of anxiety. Of these the presence or absence of symptoms was the most prominent. Participants without symptoms often took this as a sign that they had not been exposed, particularly given the dramatic symptoms experienced by Litvinenko. For participants who had had symptoms, however, concern and uncertainty tended to be higher.

Anxiety was also related to the perceived likelihood of exposure, with perceptions being driven by the participant’s temporal or physical proximity to Litvinenko. For example, one participant commented that “I read that the guy who was killed was there at

Table 3) Perceptions of incident in which Alexander Litvinenko was poisoned with polonium-210 (210Po) in London as predictors of perception that personal health is at risk

<table>
<thead>
<tr>
<th>Variables</th>
<th>No (%)</th>
<th>No (%) perceiving health at risk</th>
<th>Unadjusted odds ratio (95% CI)</th>
<th>Adjusted odds ratio (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Terrorism</td>
<td>140 (15)</td>
<td>31 (22)</td>
<td>3.3 (2.0 to 5.4)</td>
<td>2.7 (1.5 to 4.6)</td>
</tr>
<tr>
<td>A public health threat</td>
<td>160 (17)</td>
<td>29 (18)</td>
<td>2.6 (1.6 to 4.2)</td>
<td>1.9 (1.1 to 3.4)</td>
</tr>
<tr>
<td>A crime, espionage, or spying</td>
<td>634 (68)</td>
<td>51 (8)</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Only one person</td>
<td>434 (46)</td>
<td>23 (5)</td>
<td>Reference</td>
<td>Reference</td>
</tr>
</tbody>
</table>

Table 3) Perceptions of incident in which Alexander Litvinenko was poisoned with polonium-210 (210Po) in London as predictors of perception that personal health is at risk

The HPA are advising anyone who has been in an area affected by 210Po to contact NHS Direct for more information. Do you think this advice was appropriate or about right? (n=978):  

<table>
<thead>
<tr>
<th>Reason for calling NHS Direct</th>
<th>No (%)</th>
<th>Unadjusted odds ratio (95% CI)</th>
<th>Adjusted odds ratio (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Over-reaction</td>
<td>76 (8)</td>
<td>1.3 (0.6 to 2.7)</td>
<td>1.4 (0.6 to 3.1)</td>
</tr>
<tr>
<td>Under-reaction or not enough</td>
<td>116 (12)</td>
<td>2.2 (1.1 to 3.6)</td>
<td>1.3 (0.7 to 2.4)</td>
</tr>
<tr>
<td>Appropriate response or about right</td>
<td>787 (80)</td>
<td>Reference</td>
<td>Reference</td>
</tr>
</tbody>
</table>

HPA=Health Protection Agency.  
Total sample size for each variable is 1000, unless otherwise stated. Samples of less than 1000 are due to refusals, “don’t know,” or “other” responses.  
*Controlling for sex, age, income, ethnicity, and religion.
about 3pm and I left about 2ish, so that was as much as I needed to know.” Another, more concerned participant commented that she had “recognised [an associate of Litvinenko] and I moved into his booth as he was leaving.” Factors such as participants washing their hands at the venue, only being in the location very briefly, having had a drink at the hotel bar, or being a regular visitor were also mentioned as moderating perceived risk and anxiety. Comparisons with other, presumably more at risk, groups were also made: “If the [restaurant staff] had tested negative [. . . ] I was pretty comfortable then that I was at no risk.” Uncertainties about the nature of 210Po caused anxiety for some, as did its radioactivity. Personality traits (“I don’t get in a flap about these things”) and fatalism (“either you had it or you didn’t, not much point in getting stressed about it”) also played a part.

Information needs
Although some participants found their calls to NHS Direct and the Health Protection Agency reassuring, others found them less helpful. The most common complaint concerned a lack of information. Comments such as “they didn’t really give much information” and “we weren’t really told very much” were typical of people’s experiences. And although callers were given general reassurance, many noted that this was no substitute for specific information. As one put it, “All they said was platitudes which were effectively meant to reassure; how reassuring they were I’m not sure.”

Participants’ information needs fell into three main areas. Firstly, there was a desire for up to date information. The daily updates placed on the Health Protection Agency’s website were praised by several participants, although many others seemed unaware that these existed. Secondly, a need for individualised information on the likelihood of exposure was often mentioned. Those who received specific information revealing that their risk of exposure was low tended to be reassured. Others who wanted to make their own risk assessment based on when Litvinenko was in the restaurant or hotel were left feeling uncertain when this information was not provided to them. Thirdly, participants wanted information about short term health effects and derived reassurance if they answered “no” to the screening questions on symptoms asked during the phone call. For example, one participant commented: “It quickly became self-evident that I was not someone who should have a concern because I had not had any of the symptoms which were on the list.” For participants who had had a symptom on the list, however, this aspect of the phone call could be more troubling.

Factors affecting the desire for testing
Thirteen of the 21 people who did not respond to the Health Protection Agency’s letter could not recall receiving it. Five others received it but did not understand that they were being offered testing. For the remaining three, plus the 10 participants who explicitly declined a test, the main reason for declining was a perception that the likelihood of exposure was low. An apparent lack of personal benefit was also cited by some (“I sort of think, well there’s nothing you can do about it, even if it’s positive”) whereas others believed that the way in which testing had been offered implied that it was not important (“It seemed a rather passive offer”). Those who accepted the offer most often cited “peace of mind” as their rationale, although pressure from friends or relatives also played a part. Participants who were at the restaurant and were not offered testing were usually quite accepting of this fact. Although a minority believed they had a right to be tested, most believed that this was “probably unrealistic since there were so many of us.” For these participants a lack of symptoms and a low likelihood of exposure were the most salient reasons for probably declining screening if it was offered, whereas peace of mind was the reason most often given for probably accepting.

Impact of test results
Most participants who were at the hotel and provided a urine sample for testing described their results as reassuring and as expected. None the less, these participants repeatedly spoke of their need for more information. Many had been told only that their results were “of no concern.” This left some confused or even suspicious and comments such as “what is ‘of no concern’? It would have been nicer to know what the polonium amount was” and “well the test results came back normal, although there’s no indication of what normal is . . . I’ve really got to take their word for it, haven’t I?” were common. The other question often raised was what the results meant for potential long term health effects. Most participants thought that “of no concern” implied that long term effects were unlikely, but many would have preferred this to have been made explicit.

Impact on life
Few participants reported that the incident had any major impact on their life. Although some mentioned heightened anxiety, this was temporary for most. Only one person reported stigmatisation as a result of the incident. Similarly, whereas five people reported feeling less safe, these feelings had limited effects on their daily lives. Many more viewed their experiences as interesting or even exciting, making comments such as “it makes an interesting story” or “everybody was rather fascinated about it” and using humour to normalise the event. Despite this, some still mentioned underlying concerns about potential long term effects.

DISCUSSION
The incident in which Alexander Litvinenko was poisoned with polonium (210Po) in London caused limited public concern about health risks, despite involving radioactive contamination. This was partly due to the perception of the incident as a spy story and to the successful communication about the restricted nature of any risk. Had the incident been
portrayed as linked to terrorism, public concern might have been greater.

Shortly after the Health Protection Agency revised its risk assessment for people attending the hotel bar where Litvinenko had been drinking, 11.7% of our cross sectional survey sample thought that their own health might have been at risk as a result of the $^{210}$Po incident. Although there was no risk to people who had not been in a contaminated location, given that radiation is consistently rated as one of the most feared environmental hazards, it is surprising that rates of perceived risk were not higher.

Two factors helped to limit perceptions of risk surrounding this incident. Firstly, the Health Protection Agency’s communication about the restricted nature of the risks associated with the contamination seems to have been successful. Although our survey suggested that public knowledge about $^{210}$Po was limited in many respects; 71% of respondents knew that there was no risk to their health if they had not been in one of the known contaminated areas. This knowledge was strongly associated with a lower likelihood of perceived risk to health. Regardless of how successful communication was about other issues surrounding $^{210}$Po, getting this single message across did help to reassure the public.

Secondly, perceptions of risk were also strongly associated with the perceived motivation of the perpetrators, with respondents who thought that the incident was related to espionage or was aimed at one person reporting the least perceived risk and those who thought that it was related to terrorism or aimed at the general public reporting the most. These associations may have been driven by concerns about possible future incidents, with previous terrorist attacks in London having been perceived as predicting another attack in the near future. And although a non-deliberate release of hazardous material might also result in further incidents as new locations are found to be contaminated, additional terrorist attacks may be more difficult for the emergency services to prevent, detect, or contain.

Although our study was not specifically designed to assess the extent of perceptions of risk in the exposed group, our finding that between 6% and 13% of respondents from the restaurant and hotel samples thought that their health was at risk suggests that such perceptions were low even here. The personal characteristics of the exposed population may go some way to explaining this: for example, 83% of our sample had yearly household incomes of more than £30 000, a factor associated with lower risk perception in our survey. This group also tended to be well educated, a factor which may have assisted the Health Protection Agency to explain the level of risk involved. A future incident involving a less affluent group may result in higher levels of concern and may require different styles of communication.

As with the general public, potentially exposed people wanted information about their risk of exposure. Although the general public could be reassured with information about the geographical containment of the incident, however, exposed people needed more precise information relating to their specific circumstances, with participants citing factors such as lack of symptoms or the amount of time spent in a location as reasons for believing that their risk was low. These factors also played a part in determining whether someone accepted or declined urine testing. Although useful in reducing anxiety, such judgments may not be valid: in particular, the absence of acute symptoms does not necessarily imply that exposure has been avoided. This may be particularly relevant in the event of future incidents involving novel or unrecognised agents, or where health impacts have a long latent period. In such circumstances, providing clearer advice about the nature or timing of health effects might help to improve the uptake of mass screening or treatment programmes, although possibly at the expense of increased anxiety.

Information needs

A common criticism from participants was that insufficient information was provided during their initial telephone contacts with NHS Direct or the Health Protection Agency. More information would have been preferred on an individual’s risk of exposure and on the implication of the presence or absence of symptoms. Obtaining up to date information about the incident was also important. These needs are broadly in line with those previously reported by focus groups concerning scenarios as a result of “dirty bombs.” Providing such detailed information is problematic during acute incidents, particularly if staff are working under time constraints, if there is a need to prioritise obtaining clinical data from a caller, or if the requested information is classified. Directing callers to an alternative source of information may tackle some of these problems. In the $^{210}$Po incident, simply informing callers about the availability of daily updates on the Health Protection Agency’s website or providing a helpline number for more detailed queries would probably have satisfied most requests for information. Providing a candid explanation as to why certain requested information cannot be provided may also help to maintain trust.

More information was also wanted about the meaning of urine test results. Advice that these were “of no concern” was perceived as unhelpfully vague. Participants wanted to know their actual numerical results and to be given a suitable reference value for comparison. Participants also wanted explicit information about what the results meant for possible long term health effects. Providing such information before starting testing might have helped to reinforce the reassurance people felt when their test results were normal. Given that some participants did not understand that testing was being offered, perceived the offer to be passive, or declined the offer owing to a perceived lack of any personal benefit, providing further information about the test at an early stage might have helped people to make a more informed choice.
Methodological issues

Public perceptions about major incidents are liable to change rapidly as new information becomes available and media reporting evolves. Obtaining a "snapshot" of public perceptions and their predictors can therefore be difficult. In this study we used quota sampling to assess possible predictors of risk perceptions. This allowed us to obtain data from a large, representative sample within a short space of time. The trade-off for this was a low response rate (9.1%). This rate is not unusual for a telephone survey based on quota samples, however, and nor is it as valid an indicator of non-participation in quota surveys as it would be in a random probability survey. None the less, it is possible that our results may have been different had a higher response rate been achieved. In particular it has been shown that responders to telephone surveys score higher on ratings of civic involvement than non-responders. As such it is possible that our sample may have been more attentive to Health Protection Agency messages than the general population and more trusting of the various agencies involved, making them less likely to believe that their health was at risk than the general population.

Response rates were less of a problem for our qualitative interviews, which were intended to explore factors that help to reassure or inform exposed people rather than to estimate the prevalence of these factors. Participants for these interviews were therefore purposively sampled from four groups of theoretical interest. Selection biases may still have affected these results, however, as we were able to interview only those people who had provided the Health Protection Agency with their contact details. It is possible that those who did not contact the agency after the 210Po incident perceived the event in qualitatively different ways. Recall bias may also have adversely affected our interview data, with participants being asked to recall their thoughts and feelings during an event that had occurred one or two months previously. It is possible that the largely reassuring information that was given out during the intervening period caused participants to re-evaluate how they had felt during the initial stages of the incident. As such, respondents may have retrospectively considered their risk to be lower.

Finally, the open ended nature of our qualitative interviews gave participants the freedom to raise concerns that might have been missed in a more rigidly structured, quantitative, interview. The purpose of these exploratory interviews was not to assess the relative importance of the factors that we identified, however, although the findings from our study may help to inform the selection of variables for a quantitative survey of any future incident.

Conclusion

Our study emphasises the importance of giving people access to detailed, comprehensible, and relevant information about risks to which they have been exposed and tests or treatments on offer. The dismissive comments of some participants about the attempts to reassure rather than to inform them and the confusion some had over their urine test results illustrates the difficulties that experts can face in providing this level of detail to a lay audience. Ongoing consultation with those on the receiving end of this information should help to prevent and correct any similar problems in the event of a future incident.

We thank Mark Gil and the participants of an international email forum on the psychosocial effects of terrorism for their comments, and William Hallman and Steven M Becker for their input. Data collection for the cross sectional survey was carried out by interviewers working for Ipsos MORI.

Contributors: GJR and SW had the original idea for the study and developed the study design with LP, RP, PR, SH, OM, HW, MC, and JS. GJR, LP, RP and PR interviewed participants in the restaurant and hotel samples. GJR and LP carried out the qualitative and quantitative analyses. GJR wrote the first draft of the paper. All authors contributed to further drafts. SW is the guarantor.

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Competing interests: OM, HW, MC, and JS are employees of the Health Protection Agency. These authors played no part in the initial analysis of the data. LP is supported by the National Institute of Environmental Health Sciences, NIH, as a Ruth L Kirschstein national research fellow (F32 ES013690).

Ethical approval: The King’s College London Research Ethics Committee approved our qualitative interviews. The Central Office for Research Ethics Committees advised that ethical approval was not required for the cross sectional survey.


WHAT IS ALREADY KNOWN ON THIS TOPIC
Effective communication of risk during public health incidents can reassure the public and provide information to those affected

WHAT THIS STUDY ADDS
Public concern about health risks after the polonium-210 (210Po) incident in London was low because contamination was seen as related to espionage and because the public understood that unexposed people were not at risk. Access to detailed and updated information is important, particularly information on personal risk of exposure and test results.

Accepted: 12 September 2007
Vaginal discharge

Des Spence,1 Catriona Melville2

Although many cases of vaginal discharge are not caused by sexually transmitted infections and do not need to be treated, common curable sexually transmitted infections can present with this symptom. Controlling the spread of sexually transmitted infections and HIV are key public health priorities worldwide.1 Recent advances are changing investigation techniques and the management of vaginal discharge. Clinicians need to be aware of emerging epidemiological data, the different presentations of vaginal discharge, and how to approach their management so that the symptom can be treated according to its aetiology (box 1).

What is a physiological (normal) vaginal discharge?
Many women have what they perceive as an abnormal vaginal discharge at some point in their lives, but usually it is just a normal physiological discharge. This is a white or clear, non-offensive discharge that varies with the menstrual cycle. Cervical ectopy can be associated with a mucoid discharge and if symptomatic is widely treated with cryotherapy or diathermy, although evidence to support the effectiveness of these treatments is poor.

What non-sexually transmitted infections cause discharge?
Bacterial vaginosis and vulvovaginal candidiasis are common; these conditions are thought to be caused by a disturbance of the normal vaginal flora. They are not sexually transmitted and the male partner does not need to be treated. A retrospective study of patients with vaginal discharge in general practice found that most were managed as candidiasis even though bacterial vaginosis is more common.3 Group B Streptococcus is often reported on vaginal swabs, but this organism is not usually thought to cause discharge and only needs treatment in pregnancy.3

Bacterial vaginosis
Bacterial vaginosis is the most common cause of infective vaginal discharge,4,5 with a prevalence of 9% in UK general practice.5 It causes profuse and fishy smelling discharge (fig 1) without itch or soreness. This condition is characterised by an overgrowth of anaerobic bacteria and occurs and remits spontaneously.7 Asymptomatic bacterial vaginosis in non-pregnant women does not require treatment.4 The condition is associated with poor pregnancy outcomes, endometritis after miscarriage, and pelvic inflammatory disease.1

Vulvovaginal candidiasis
The prevalence of asymptomatic carriage of Candida in women is 10%.8 Symptoms are vulval itch and soreness and thick white non-offensive discharge (fig 2). There is no evidence that combined oral contraceptives cause candidiasis. Asymptomatic vulvovaginal candidiasis does not need treatment.9

What sexually transmitted infections present with vaginal discharge?
Chlamydia trachomatis, Neisseria gonorrhoeae, and Trichomonas vaginalis can present with vaginal discharge but may also be asymptomatic. These infections are associated with an increased risk of HIV transmission, especially in the developing world.10 Rates of sexually transmitted infections are rising in the United Kingdom11 and elsewhere, but this observation may be confounded by increased awareness, increased testing, and, importantly, new laboratory techniques.12 Basic epidemiological data about these infections—such as point prevalence, lifetime incidence rate, complication rate, and natural clearance—are scarce for the general population.

<table>
<thead>
<tr>
<th>Causes of vaginal discharge</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Non-infective</strong></td>
</tr>
<tr>
<td>- Physiological</td>
</tr>
<tr>
<td>- Cervical ectopy</td>
</tr>
<tr>
<td>- Foreign bodies, such as retained tampon</td>
</tr>
<tr>
<td>- Vulval dermatitis</td>
</tr>
<tr>
<td><strong>Non-sexually transmitted infection</strong></td>
</tr>
<tr>
<td>- Bacterial vaginosis</td>
</tr>
<tr>
<td>- Candida infections</td>
</tr>
<tr>
<td><strong>Sexually transmitted infection</strong></td>
</tr>
<tr>
<td>- Chlamydia trachomatis</td>
</tr>
<tr>
<td>- Neisseria gonorrhoeae</td>
</tr>
<tr>
<td>- Trichomonas vaginalis</td>
</tr>
</tbody>
</table>

Box 1

1Maryhill Health Centre, Glasgow G20 9OR
2Sandyford Initiative, Glasgow G3 7NB
Correspondence to: D Spence destwo@yahoo.co.uk
BMJ 2007;335:1147-51
doi:10.1136/bmj.39378.633287.80
Chlamydia trachomatis is the most common sexually transmitted infection caused by a bacterium in the UK. Around 5-10% of sexually active women under 24 years are infected. Chlamydia can cause a purulent vaginal discharge, but it is asymptomatic in 80% of women. It was thought that 10-40% of untreated chlamydial infections will result in pelvic inflammatory disease. This has recently been challenged by a large observational study, which reported that only 5.6% of women developed this disease, and by a small prospective study that reported an even lower rate of 1%. Clearly this has implications for information given to patients and screening programmes.

Neisseria gonorrhoeae may present with a purulent vaginal discharge but is asymptomatic in up to 50% of women. The true prevalence and epidemiology in the general community is not known. Gonorrhoea may be complicated by pelvic inflammatory disease.

Trichomonas vaginalis can cause an offensive yellow vaginal discharge, which is often profuse and frothy, along with associated symptoms of vulval itch and soreness, dysuria, and superficial dyspareunia, but many patients are asymptomatic. This infection is associated with preterm delivery. The true prevalence and epidemiology in the general community is not known.

What about concurrent sexually transmitted infections?
The presence of one sexually transmitted infection makes the presence of other infections more likely, but this depends on the population studied. For example, in a recent large community screened population in the Netherlands, only 0.2% of woman diagnosed with Chlamydia had concurrent gonorrhoea. In contrast, up to 40% of women diagnosed with gonorrhoea have a coexisting chlamydial infection. Women who have one sexually transmitted infection are likely to have another, including HIV and syphilis, but the role of routine screening for these infections is not established in the literature.

What are the key features from the history?
Features of the discharge such as its timing, colour, consistency, smell, and presence of itch are important in distinguishing between infections. Pelvic pain, pelvic tenderness, and fever should be considered as red flags for pelvic inflammatory disease. Taking a sexual history will help identify patients at high risk of a sexually transmitted infection (young women, those with a recent change of partner, those who have unprotected intercourse, and those who have multiple partners). The need for examination and investigations is usually determined on the basis of such a history. It is important to elicit the patient’s “agenda” and explore health beliefs because much social stigma and many lay misconceptions surround sexual health.

What examination is needed, and when?
A vaginal examination using a speculum is often done routinely when a patient presents with vaginal discharge. However, in many situations this is not possible, it is also invasive, and it often does not inform initial management. New sampling techniques may negate the need for vaginal examination in low risk and uncomplicated presentations. Recent General Medical Council
guidance on intimate examinations suggests a “chaperone” be offered, even when the examiner is the same sex as the patient. In the management of vaginal discharge, routine bimanual vaginal examination lacks supporting evidence and this examination is only indicated if there is concern about pelvic inflammatory disease.

What tests should be done?
Guidance from the Faculty of Sexual and Reproductive Healthcare and the British Association for Sexual Health and HIV indicates that patients who present with symptoms suggestive of bacterial vaginosis and vulvovaginal candidiasis can be treated without sampling. Whether or not samples are taken, when they are taken, and what type of samples are taken depends on the resources, the patient, and the clinical setting.

“Triple swabs” (box 2) should be taken—a randomised controlled study of 200 women presenting with vaginal discharge showed that the addition of a high vaginal swab for culture provided a more accurate final diagnosis than the use of microscopy alone. If transport of samples is delayed they should be refrigerated.

Vaginal pH testing (using narrow range pH paper) is a quick, cheap, and simple test that can help discriminate between the two most common causes of vaginal discharge—bacterial vaginosis (pH >4.5) and vulvovaginal candidiasis (pH <4.5). In one study, pH testing alone had a sensitivity of 73% for the diagnosis of bacterial vaginosis, but in combination with clinical symptoms this rose to 81%.

Which new tests are becoming available?
Nucleic acid amplification tests, such as polymerase chain reaction and ligase chain reaction, are molecular biological techniques that amplify DNA and other genetic material. These tests can detect tiny amounts of cells or viruses and are highly sensitive and specific.

A recent systematic review of these tests on urine specimens found high specificity (95%) and sensitivity (80-93%) for detecting Chlamydia and gonorrhoea (sensitivity was lower for gonococcal infections in women using polymerase chain reaction). This increased sensitivity was also demonstrated in a large

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**Box 3** Management of vaginal infections

### Bacterial vaginosis
- Metronidazole 2 g as a single oral dose, metronidazole 400-500 mg twice daily for five to seven days, intravaginal clindamycin cream (2%) once daily for seven days, or intravaginal metronidazole gel (0.75%) once daily for five days
- The infection often recurs and acidic vaginal jelly (such as Relact from Kora Healthcare) may reduce relapse rates
- Partner notification not needed

### Vulvovaginal candidiasis
- Vaginal imidazole preparations (such as clotrimazole, econazole, miconazole—various preparations are available including single dose ones), or fluconazole 150 mg orally
- The role of alternative treatments like tea tree oil and yoghurt containing Lactobacillus acidophilus have not been evaluated
- Oral versus vaginal treatment depends on preference
- Treatment for candidiasis is available over the counter in the UK
- Partner notification not needed

### Chlamydia trachomatis
- Doxycycline 100 mg twice daily for seven days (contraindicated in pregnancy), azithromycin 1 g orally in a single dose (WHO recommends azithromycin in pregnancy but the British National Formulary advises against its use unless no alternatives are available)
- A test of cure is not indicated
- Partner notification required

### Gonorrhoea
- Cefixime 400 mg as a single oral dose or ceftriaxone 250 mg intramuscularly as a single dose
- Referral to a genitourinary medical unit is encouraged because of the existence of resistant strains of the organism
- A test of cure is not routinely indicated if an appropriately sensitive antibiotic has been given, symptoms have resolved, and there is no risk of reinfection
- Partner notification required

### Trichomonas vaginalis
- Metronidazole 2 g orally in a single dose or metronidazole 400-500 mg twice daily for five to seven days
- Partner notification required

Readers should refer to BASHH guidelines, the British National Formulary, and local policies for full treatment options, including treatment in pregnancy.
observational cohort study of women attending a genito-urinary medical service, where use of molecular techniques was associated with an increased detection rate of Chlamydia compared with traditional culture (9.9% v 6.1%). Commercial assays are available for C trachomatis, T vaginalis, N gonorrhoea, C albicans, GBS, and herpes simplex viruses 1 and 2, and some of these assays give real time rapid results. Molecular based sampling has cost implications and tests remain positive for several weeks after treatment. Furthermore, no antibiotic sensitivities are available and a confirmatory culture is needed after a positive molecular test for gonorrhoea.

**What is the role of self taken swabs and urine testing?**
Molecular tests can use non-traditional samples. Self taken vaginal swabs, urine samples, and clinical tampons have shown comparable results to traditional vaginal specimens. These methods are more acceptable to patients, and in a large questionnaire study 76% of respondents preferred self taken swabs and 94% stated they would be willing to be tested more often if self taken swabs could be used. Such specimens also negate the problems associated with chaperones. The potential for testing using non-clinic based environments is enormous (for example, postal kits), and these techniques are in the process of being validated in clinical practice.

### ADDITIONAL EDUCATIONAL RESOURCES

**Resources for healthcare professionals**
- British Association for Sexual Health and HIV (www.bashh.org/guidelines.asp)—Series of guidelines on sexual health
- Clinical Evidence (www.clinicalevidence.com)—A medical resource for informing treatment decisions and improving patient care
- Faculty of Sexual and Reproductive Health Care (www.ffprhc.org.uk)—This organisation provides information and a clinical advisory service on sexual health
- Medical Foundation for AIDS and Sexual Health (www.medfash.org.uk)—This organisation works with policy makers and health professionals to promote excellence in the prevention and management of HIV and other sexually transmitted infections

**Resources for patients**
- FPA (www.fpa.org.uk)—Information for professionals and patients. The leaflet “Bodyworks” is particularly useful
- Clinical Knowledge Summaries (www.cks.library.nhs.uk/patient_information/browse_all_leaflets)—Evidence based clinical knowledge on common conditions managed in primary and first contact care. The site provides useful information leaflets for patients
- Best Treatments (www.besttreatments.co.uk)—Website that rates thousands of health and medical treatments on the basis of how well they work

**SUMMARY POINTS**

Vaginal discharge is caused by non-sexually and sexually transmitted infections

- Non-sexually transmitted infections may not need treatment, but sexually transmitted ones must be treated and partners notified
- Recent research suggests that fewer women with untreated chlamydial infection may develop pelvic inflammatory disease than previously thought—only 1-5.6%
- Concurrent infection depends on the population studied
- Molecular techniques are more sensitive than culture but are expensive, do not provide antibiotic sensitivities, and results can remain positive after treatment
- Self taken vaginal swabs, urine samples, and clinical tampons show comparable results to traditional vaginal specimens

**What are the recommended treatments?**
Box 3 summarises some of the recommended treatments for individual infections.

**What about resource poor countries?**

In countries that lack laboratory services, the World Health Organization promotes the use of “syndromic management” of vaginal discharge. Algorithms are used to assess the probability of infections on the basis of history and examination, and patients are treated empirically on this basis. This pragmatic approach has helped reduce the spread of HIV.

**Hygiene advice**

Patients should be advised to avoid using local irritants, like perfumed soaps and shower gels, and to be wary of feminine hygiene products such as wipes, powders, and sprays, which may upset the vaginal flora or cause allergic reactions. Vaginal douching should be avoided as it is associated with bacterial vaginosis and pelvic inflammatory disease.

**What about partner notification?**

Partner notification of recent sexual contacts is considered essential both nationally and internationally to prevent the spread of sexually transmitted infections including HIV. A recent systematic review, however, commented on the poor quality of the available data, but highlighted the need to involve the patient in sharing responsibility. Consider using patients to deliver partner therapy, allowing home sampling for partners, and providing additional information for partners. A large randomised controlled trial of nurse led, primary care based partner notification proved this to be feasible, effective, and no more expensive than specialist services.

**When should I refer patients?**

Most patients presenting with vaginal discharge will have either a physiological or a non-sexually transmitted infective cause, and these can be managed...
within primary care. Uncomplicated sexually transmitted infections can be managed in primary care with the support of specialist services, particularly with regard to providing partner notification. Specialist referral should be considered for women with recurrent discharge, pregnant women, or women whose discharge is complicated by pelvic pain. Near patient microscopy, available in many specialist services, is a useful diagnostic tool. Access to sexual and reproductive health services is important, and this is reflected by the location of services within the community and the self referral or drop-in approaches offered by many clinics in the UK.

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PRACTICE

A PATIENT’S JOURNEY

Pemphigus vulgaris

Siri Lowe

Twelve years ago, Siri Lowe developed pemphigus vulgaris, a potentially fatal autoimmune blistering disorder. As her story shows, it can have a devastating impact on patients’ lives, as can the side effects of the necessary treatments.

When my mouth and tongue suddenly became badly blistered in 1995, I never suspected there could be anything seriously wrong with me—this was surely just some crazy infection in my mouth. But it was pemphigus vulgaris, a rare, life threatening, autoimmune disease affecting skin and mucous membranes, and, of course, I’d never heard of it in my life.

I deteriorated quickly and in only five weeks moved from being strong and healthy to being unable to eat solid food, drinking through a straw, and being in agonising pain. I remember walking the London streets in a total daze thinking, “This can’t be true, it’s like the script of a bad television play.” I had no idea how living with a chronic disease would change my life.

There’s no cure for pemphigus. No smart drug to take it all away. It is nearly always controllable, but that control comes at a heavy cost. At that time, my only options were high dose corticosteroids or heavy immunosuppressant treatment. Not only had I a life threatening disease but my future suddenly became ruled by serious prescription drugs.

The early days

During the first three years, the drugs themselves brought their own health problems, some serious and some just hard to live with. I was hugely grateful that my disease wasn’t as bad as some people’s—at least my skin hadn’t literally blistered off my body—but it gradually began to affect nearly every area of mucous membrane: mouth, nose, throat, eyes, vagina, cervix.

Coping with the condition was extremely difficult. The slightest change in drug regimen could disturb the precarious balance, and instead of controlling the disease I’d be tumbling down into another crisis. Those years were a constant nightmare until my consultant dermatologist found a drug combination that I could tolerate and which worked (with only minor flares).

I secretly hoped my “journey” would be over once I got this far. Consequently, I found it very hard to accept that my health was badly damaged and I couldn’t return to my old self. High dose corticosteroids and immunosuppressants had been necessary, and undoubtedly saved my life. But there were side effects, and I was now disabled with problems with walking and pain. Prescription analgesics and pain management techniques could do no more than modify the pain levels. I had changed.

Six months after becoming ill, it became clear I couldn’t return to work. I had to retire. Suddenly I was no longer part of a dynamic publishing company. I was also far too ill to continue with the voluntary work I’d trained to do, and the hobbies I’d enjoyed before were now either physically impossible or too exhausting. By the time my condition was more stable, I’d lost many of the things that defined who I was. I’d lost my financial viability and my identifiable role in the world. I was also a claimant, constantly worrying about the next set of forms to be filled in. All I had was the illness. I was an illness and nothing but an illness.

The people around me

But that’s the downside. I also had wonderful companions. My surviving family were elderly and frail and needed to be protected from some of the unpleasant facts, but I had the constant presence of many loving and supportive friends. With them, I was able to explore new ways of relating to people. I’d usually been the “helper.” Now I had to learn to accept help, and it wasn’t an easy lesson. I started to realise that I could still have a sense of identity but that it would have to be a different one.

USEFUL RESOURCES

- International Pemphigus & Pemphigoid Foundation (www.pemphigus.org) in the US has an excellent medical advisory board; provides information and support; offers an email discussion group and online live chat.
- Pemphigus Vulgaris Network (www.pemphigus.org.uk) is the support group started for the UK, which provides information and support and focuses on things specific to the UK (we work closely with the International Pemphigus & Pemphigoid Foundation).
- The Electronic Medicines Compendium (www.emc.medicines.org.uk) gives full and up to date drug information, essential for pemphigus patients, and is produced by the Association of the British Pharmaceutical Industry (ABPI).
- The Skin Care Campaign (www.skincarecampaign.org) for the wider picture of issues affecting pemphigus patients.
A doctor’s perspective

Pemphigus is a serious autoimmune blistering disorder caused by circulating autoantibodies to the epithelial adhesion proteins desmoglein 1 and 3. These antibodies result in a failure of epidermal cells to adhere correctly to each other. This causes flaccid blisters and subsequently painful erosions in the skin and mucous membranes.

Before the introduction of systemic glucocorticosteroids in the early 1950s, pemphigus was a universally fatal disorder with extensive involvement of the skin and mucous membrane leading to prostration, sepsis, and failure of multiple organs. The use of steroid sparing immunosuppressants such as azathioprine, cyclophosphamide, methotrexate, and ciclosporin has been the turning point in the management of the disorder. Recently, rituximab (an anti-CD20 antibody which targets B cell differentiation) administered together with intravenous immunoglobulin has been shown to be another advance. Pemphigus is therefore now eminently treatable.

Ms Lowe’s account does show, however, just what an unpleasant disorder pemphigus vulgaris is, and what a tremendous toll it has taken on her personal life. She describes how completely devastated she was by the diagnosis and how the treatment, particularly systemic corticosteroids, interfered with her wellbeing. She also had ready access to information particularly via the internet, and this must have been quite frightening to read.

As the physician central to her case for the past 10 years, I have found my role to be largely guiding Ms Lowe through her illness and adapting the use of steroids, azathioprine, and ciclosporin to fit her personal needs. It was possible to induce a complete remission fairly early on, although she did have a relapse five years ago, and she still worries that she might relapse again. During this time, she has also developed breast cancer, and was clearly concerned what effects surgery and intubation during anaesthesia might have on the disease. The dermatologist working in the hospital was able to liaise with her other specialists, explain her condition, and orchestrate her care, so that she managed psychologically to survive the trauma of her second illness. The lesson that was reinforced to me about caring for her and for most patients with serious skin disorders is how essential adequately resourced specialist dermatology services are.

Ms Lowe has fought her illness with great fortitude. A measure of this has been the determination with which, with the support of the British Association of Dermatologists, she set up the first patient support group for pemphigus, which has been of immense help to other people with the condition.

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One of the ways this happened was as a direct result of my condition. In the early days one of the things I had found most difficult was getting any information about pemphigus and what it was like to live with. How many people survived? Did everyone feel as awful as I was taking the drugs? Each friend inevitably had to explore the International Pemphigus Foundation in the United States, and I was able to get those myriad questions answered. It was so much easier to cope once there was someone else with pemphigus to correspond with. I still remember that sense of relief. So, together with friends, I started the UK patient support group, which is still running today.

Of course, my constant companions are the doctors who look after me, primarily my consultant dermatologist, who has stayed consistently committed to my care. Because pemphigus has affected my body in so many different ways, I also see seven other consultants in four different hospitals. Miraculously, I’ve mostly been able to stay with the same specialists. This continuity makes such a difference. It’s grim enough spending so much time waiting in hospital outpatient clinics, but it’s really awful having to explain, yet again, to yet another doctor, the problems that are important to me. Hospital notes should do this, of course, but somehow they never do.

Other serious medical conditions have added to the difficulties. I’ve had breast cancer in both breasts—five operations, radiotherapy, etc. Suddenly I can find myself seeing doctors or nurses who don’t believe a skin disease is serious. At times it seems impossible for people to see that my needs as a cancer patient can’t be dealt with in isolation from my needs as a pemphigus patient. My calm dissolves in the insanity of trying to communicate with a health professional who doesn’t believe patients can know what they’re talking about. I just have to remember all the fantastic doctors and nurses who can see the wider picture. Luckily this problem doesn’t occur often.

WHAT WORKS WELL AND WHAT DOESN’T

What works well

• The therapeutic alliance between doctor and patient when it happens. I don’t know how I could have got through the past 12 years without the close alliance I have with my doctors, particularly my consultant dermatologist. I’m convinced it increases my healing resources and helps get me through the worst times. There doesn’t seem to be a channel to thank any of them properly—which is a pity.

• Continuity of care. In the changeable world of pemphigus I need the stability of the same doctors treating me over a period of time and knowing my case.

• When doctors cut through bureaucratic red tape to share essential information, such as an ear, nose, and throat specialist contacting an anaesthetist regarding special procedures.

What works less well

• There’s no psychological space to say how scared I am—permanently. I think I’d risk almost anything else happening rather than go back to that terrible place of pemphigus crisis—skin dissolving, unbearable pain, and 80 mg/day of steroids.

• When people don’t take pemphigus seriously. For example, it doesn’t matter how brilliant surgery is if healing is messed up in a hospital ward where no one listens if I say, “I’m immunosuppressed, you need to be really careful about infections,” “I’ve got a serious skin condition, if you use that dressing I’ll have a bad reaction.” This is the downside of health care—when the patient isn’t believed and Skin disease doesn’t count as important. Not only is it physically dangerous, but it pushes me to a point of emotional despair which hasn’t got easier over time.

• Confusion of language. When doctors talk about “remission” they mean disease control with drugs, but the rest of us think remission means a cure and no further need for drugs.

• The pressure to always be positive. No one wants a “heartsink” patient, that was made clear to me very early on. So I end up saying I’m doing well when what I mean is that the pemphigus is doing well, but the unwanted effects of my drugs mean I feel awful most of the time.
Where am I now?
I’ve learnt to live in new ways: to celebrate the good days and try to use them. Equally, I have to accept the bad times—even if that means days or weeks when all I can be is the “sick” person. My condition can change rapidly, so I have to stay ready to adapt within days.

Emotionally it’s hard to shift paradigms at the drop of a hat. There’s no point being permanently optimistic, for then it feels catastrophically painful to slip down again. Conversely, there’s no point being permanently pessimistic, for then there’d be no joy in life, no possibility of experiencing each moment for itself.

I would love to have been more upbeat describing this journey, but the truth is more complex. Of course, I hope that medicine will provide a real cure, though there’s no scientific indication of that on the horizon. So I can only hope that pemphigus, the drugs, pain, and disability will leave me enough space to live an altered, but still worthwhile, life.

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LESSON OF THE WEEK
Alcohol hand rubs: hygiene and hazard

John R H Archer,1 David M Wood,1 Zoe Tizzard,1 Alison L Jones,2 Paul I Dargan1

Young or confused people and those dependent on alcohol are at risk from ingestion of alcohol hand rubs together with data from our poisons unit showing an increase in inquiries related to alcohol rubs.

Case report
A patient known to have a history of alcohol dependency presented with withdrawal symptoms, having not consumed alcohol for 24 hours. On examination the patient was alert, orientated (with a Glasgow coma score of 15/15), with tachycardia (95 beats/min), tremulous, and sweaty, but with no focal neurological abnormalities. Intravenous thiamine and chlordiazepoxide were started under the hospital alcohol withdrawal protocol. During this admission, the patient was found collapsed (coma score 3/3), having vomited in the bathroom, holding an empty 500 ml bottle of alcohol hand rub, and lying next to another such bottle (preparation 4 in the table).

The patient was intubated and ventilated and transferred to the intensive care unit, where intravenous antibiotics were started for aspiration pneumonia. Computed tomography of the head was normal, and blood ethanol concentration at the time of collapse was 7 g/l (152.2 mmol/l). This is nine times over the legal UK driving limit (0.8 g/l) and is a potentially fatal concentration.10 The patient was normoglycaemic and had normal renal function; liver function tests were in keeping with chronic alcohol excess, and she had a mild metabolic acidosis. On questioning after extubation, the patient denied any intent to self harm.

We searched the Guy’s and St Thomas’ Poisons Unit’s database to compare the numbers of inquiries related to both children and adults exposed to alcohol hand rub (both ingestion and eye exposure) during the 16 month periods before and after the widespread introduction of alcohol hand rubs (December 2003 to March 2005 and April 2005 to July 2006 respectively). The search found an
increase in the total number of inquiries about alcohol rub (from 23 to 30) to the poisons unit. However, when the total general call rate to the poisons unit is taken into account, there is also a large proportional increase (303%) in the total number of inquiries relating to exposure between the two periods (P < 0.01). Here the most marked increase, 314% (7 vs 29 inquiries), was in adult ingestion numbers (intentional and unintentional), 66% (19) of which were thought to be the result of intentional ingestion. All cases of ingestion occurred within hospitals or care homes. Unintentional ingestion occurred in very young people and in elderly people and in those confused, whereas intentional ingestion occurred only in those with alcohol dependency.

**Discussion**

The NHS Purchasing and Supply Agency have five alcohol hand rub products available (table). These products contain varying quantities of hydrogen peroxide and other ingredients (but all in smaller quantities than ethanol and isopropanol). However, the main risk from ingestion is the potential for ethanol and/or isopropanol poisoning.

We have had inquiries about all five types of preparations, including those containing denatonium benzoate (a bittering agent, which would make preparation less palatable). Isopropanol may occur in concentrations as high as 30% and can cause effects similar to those of ethanol. Depending on previous tolerance to ethanol, deaths have been associated with ingestions of 100-250 ml of a 70% isopropanol solution.11 12 The adverse effects of ethanol are variable, with chronic ingestion causing tolerance to high blood ethanol concentrations as an adaptive process.13 Survival in patients with very high blood ethanol concentrations (>10 g/l) has been reported.14

Owing to the wide variation in individual response and tolerance to ethanol, a “toxic dose” of alcohol hand rub is difficult to establish. However, in a normal adult as little as 360 ml of an alcohol hand rub containing 80% ethanol could potentially lead to life threatening complications, but this will vary depending on previous exposure to ethanol.10

After exposure to an alcohol hand rub clinical effects generally occur within 1-2 hours of ingestion. The most common adverse effects are those of ethanol intoxication, including epigastric pain and vomiting. More serious effects involve depression of the central nervous system, leading to aspiration and respiratory arrest. If a patient develops symptoms, medical attention should be sought. Management is largely supportive, although if a large volume of hand rub is thought to have been ingested, close observation is required in case of ensuing depression of the central nervous system and its sequelae. In our experience the more serious effects are seen in those who ingest more than 500 ml of hand rub, and this is most likely to occur in confused patients (such as, they may mistake it for water) and those with alcohol dependency seeking the desired effect.

Similar gel-like hand sanitisers containing alcohol have been used by inmates in correctional facilities in the United States to generate more palatable ethanol by passing alcohol rub through simple table salt contained in a sock.15 This further highlights the potential for misuse of these products.

Poisoning from alcohol hand rub remains relatively uncommon but has increased since widespread introduction of the hand rubs in the UK. Potentially serious clinical effects can occur with ingestion. With the wide distribution of these products in hospitals, the possibility of unintentional exposure, self harm, and misuse is more apparent. This is particularly important in patient areas that are easily accessible by those thought to be at high risk of ingestion. In these areas the larger hand rub dispensers (>500 ml) could be placed within locked secured holders preventing unintentional or intentional withdrawal of the container and ingestion. This potential for toxicity presents a major challenge to patients’ safety and to risk management, which needs a multidisciplinary and coordinated approach from risk managers, toxicologists, and infection control specialists.

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Why is Exubera being withdrawn?

PERSONAL VIEW Clifford J Bailey, Anthony H Barnett

On 18 October Pfizer announced that it would withdraw the first inhaled insulin, Exubera, from the market, as sales were too low. In January 2006 Pfizer bought the worldwide rights to Exubera from Sanofi-Aventis for $1.3bn (£0.6bn; €0.9bn), and in August 2006 the product was introduced in Britain. In the first nine months of 2007, worldwide sales of Exubera amounted to $12m, rather short of its projected $2bn blockbuster status. Instead it will cost Pfizer an estimated $2.8bn to “write it off.”

So why were sales of Exubera so far below expectations? Was it that labelling and national guidance were too restrictive? Did Pfizer not persist long enough for the market to open up? Was the cost too high? Was the inhalation device less convenient than anticipated? Was the dose equivalence confusing or inaccurate? Were there doubts over its long term safety? Was it because temporary cough can be irritating? Was it none, some, or all of the above?

Exubera’s withdrawal has implications for the companies that make the insulin and the inhalers, as well as Nektar Therapeutics, which developed the inhaler. Nektar has yet to announce how it will proceed. Several other companies have inhaled insulin products in development, including Eli Lilly, Novo Nordisk, and the MannKind Corporation, and it is not yet clear how the withdrawal will affect these programmes, although the companies have said they intend to continue.

In principle the lungs offer several opportunities for the delivery of peptides. Their large surface area aids rapid absorption, administration is painless, and trial participants who use Exubera have reported a high level of satisfaction and acceptability. After careful evaluation, the US Food and Drug Administration and the European Medicines Agency were sufficiently satisfied about the product’s safety to grant a licence, although with some important exclusions (such as cigarette smokers, people with major pulmonary disease, and children) and a requirement for pulmonary function testing before patients started Exubera and then at intervals afterwards.

We believe this to be the first time that a licensed product for managing a common chronic disease has been withdrawn from the market so quickly for what would seem to be purely economic reasons. Despite any criticisms that might be levelled at Pfizer’s marketing strategy, and practical difficulties with the device itself, it seems that restrictive guidelines may have contributed to the poor sales. In its preliminary consultation document the UK National Institute for Health and Clinical Excellence (NICE) did not recommend the use of Exubera at all, saying that cost effectiveness had not been shown. After comments from groups such as Diabetes UK, the Association of British Clinical Diabetologists, and various nurses’ organisations, NICE softened its attitude and recommended use of Exubera, but only in patients with a true needle phobia or where there were major needle site problems (www.nice.org.uk/TA113quickrefguide).

The conclusions of NICE and similar bodies recommending Exubera only in restricted cases should send a warning to drug companies that their development programmes should look beyond what is needed to gain a licence: their studies may have to demonstrate cost effectiveness of the product and use in “real life” clinical practice situations. This may not be easy in the case of drugs for chronic diseases, given that hard data on outcomes are unlikely to be available by the time of the launch, so that surrogate end points may still be needed to demonstrate cost utility.

NICE guidance and labelling restrictions made it almost impossible for clinicians to prescribe Exubera to many UK patients who might have benefited from this new technology, including people with poorly controlled type 2 diabetes who refused to start insulin treatment because they did not want to inject (rather than those with true needle phobia) and those with type 1 or type 2 diabetes who needed to intensify insulin treatment to improve control but would not do so because it would mean more injections.

What do we do about our patients who already take inhaled insulin? One of us (AHB) runs an inhaled insulin clinic for patients who fulfil the NICE criteria. The response among those who have been prescribed Exubera has been almost universally positive. What are we to tell them? The lifeline that they have been offered and have taken up has now been cruelly removed, and they will have to wait at least two years for alternative products to appear. We also have several patients who have been promised access to this new technology and who now have to be told that it is no longer available.

Perhaps more worrying, however—if the decision on Exubera is indeed solely economic (as seems to be the case)—is that drug companies may now be less inclined to speculate on the development of new products unless there is greater assurance over reimbursement. As a result the industry may reduce its commitment to research and development of novel compounds and concentrate in other areas, such as “me too” products. The appetite to invent and develop novel treatments may be suppressed. This is in nobody’s interest, least of all our patients’.

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A longer version of this article with references is on bmj.com
It is no news that science is messy. Louis Pasteur said it most famously: “Chance favours the prepared mind.” His compatriot the physiologist Claude Bernard chimed in with: “Experimental ideas are often born by chance.” The Nobel prize winner Peter Medawar probably argued it most subtly, when he wrote a paper, cheeky but serious, announcing that the scientific paper is a fraud. Medawar wasn’t a whistleblower; he merely analysed, in his inimitable style, the fact that scientific papers routinely present the route to their results through a series of logical experiments, correct deductions, and obvious conclusions. In practice, things rarely go as expected. Abortive experiments are abandoned, and results are tidied up to be presented in their strongest form. This is normal experimental practice, although it took someone of Medawar’s stature to make it public quite so blatantly.

It is significant that Morton Meyers draws his examples from major medical innovations and can usually draw on the authors of those discoveries to confess that something went wrong or that they found results they were not looking for. It is easy to confess that things were not all that neat when the result has won the researcher fame (and, often, fortune).

The phenomenon of serendipity in science and medicine is well known, but Meyers has collected a particularly well populated group of such discoveries and presented them in a chatty, readable fashion. In four sections he exposes the role of chance in the discovery of antibiotics, anticancer drugs, cardiovascular innovations, and psychopharmacology. The familiar examples are all here: Fleming’s exposed petri dish leading ultimately to penicillin; Waksman’s work with soil bacteria that turned up streptomycin; the road from nitrogen mustard gas to cancer chemotherapy or from spoiled clover to coumarin.

Meyers has also scoured the literature and uncovered some less well known examples. Nearly all of the physical treatments in psychiatry seem to have been stumbled on. Short chapters detail the centrality of chance in the introduction of fever therapy for treating general paralysis of the insane, chemically and electrically induced shock, lobotomy, lithium, chlorpromazine, mephenesin, monoamine-oxidase inhibitors, tricyclic antidepressants, fluoxetine, chlor diazepoxide, diazepam, disulfiram, and LSD. In each case someone noticed something unexpected in the laboratory or clinic and was able to develop the observation further—or at least publish the paper that allowed others to do so.

Meyers has an eye for detail and anecdote, and the book is an excellent read. To his credit he unfolds his story within a reasonably sophisticated philosophy of discovery. We are treated to the role of “normal” and “revolutionary” science, as developed by Thomas Kuhn. One gets the impression that Meyers is no fan of the medical paper with 50 or more authors. Creativity, not teamwork, is the hero of this monograph.

Occasionally Meyers exaggerates the role of serendipity. For instance, Julius Wagner-Jauregg, who won a Nobel prize for his work on malaria in 1927, knew, as did many psychiatrists of the 1910s, about reports of psychotic patients improving after a bout of fever. His creativity, such as it was, lay in devising a controlled way of giving patients a high temperature with vivax malaria, which could then be treated with quinine.

The messiness of modern drug discovery and marketing gets fairly short shrift in this account. Meyers is more likely to tell us how many Americans are taking anticoagulants, antidepressants, or tranquillisers, or what the first billion dollar cancer drug was than about side effects, inappropriate prescribing, or dubious claims by drug companies. When we do get such information it is presented in the blandest of terms, quite unlike the tone when Meyers describes original observations.

His cosy blandness is partially redeemed in his last chapter, when he castigates the pernicious lobbying and direct advertising strategies of modern drug companies in the United States. Even here Meyers blames but two of the three guilty parties: companies, for their conscious lobbying and direct advertising strategies; doctors, too, have a responsibility, notwithstanding Meyers’ cogent criticisms of the US style medical marketplace.

W F Bynum is impressed by a book about the role of chance in medical innovations.
May the force be with you

“Use the force, Luke. Let go!” He turned off his targeting computer—certain folly! But the torpedoes went down the ventilation shaft and Death Star, the most advanced weapon to threaten the universe, exploded. The whole cinema whooped. My brother and I spent the next few years imaging we were duffle coated Jedi knights, following the code and saving the universe, and mimicking the noises and voices of *Star Wars*. I am not sure whether I still believe in the force, but I do believe in something even more unlikely: clinical intuition.

It is hard to explain the ancient power of clinical intuition to the young “padawan” of the i-generation, whose only faith is the binary code of the microchip. But a few of us still believe. You can spot them: in general practice their garb is brown corduroys or tweed skirts and jackets with leather patches. In the hospital their trousers are too short and they wear the same shirt every day, but it is their footwear—comfortable brown Clark’s shoes—that marks them apart. Understated and seemingly invisible, they quietly get on with clinical commitment in all the unfashionable corners of the NHS. Their colleagues, especially the young ones, shackled by evidence based medicine, smirk at their mumbled ancient incantations, such as, “That just doesn’t fit with the story,” and, “There’s something else going on.”

But over many thousands of clinical contacts some vividly stand out where clinical intuition saved the day. Intuition is hard to put into words but is a sense that something somehow is just “not right.” It is a change in the smooth and regular wave forms that radiate from patients—perhaps a change in the tone, pitch, or pace of their voice or a change in posture. But really intuition is just a feeling, a disturbance in the clinical force. These odd experiences are shared by many of us but are spoken of only in hushed voices, for fear of being overheard.

Clinical intuition is stronger in some people but is present in all of us. It is just a question of tuning in, letting go, and trusting. But this is medical heresy in these days of the randomised controlled trial and systematic review, in this evil empire of technological medicine. However, I will try to instruct students in the old ways for as long as I can, before the Empire’s stormtroopers close in and I face banishment to the desolate planet of Protocol.

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Homoeopathy and the star that fell

Some are born great, some achieve greatness, and some tragically squander greatness in a hopelessly misguided obsession, launching centuries of self delusion. Take Samuel Hahnemann. Born in Meissen in 1755, he displayed early brilliance in languages before opting to study medicine, graduating in 1779. Rapidly disillusioned by the barbaric practices of the day, Hahnemann condemned his peers’ ignorant reliance on copious bloodletting, toxic purges, and caustic enemas. By contrast Hahnemann advocated the healing effects of a sensible diet, fresh air, plentiful exercise, and routine hygiene as “the preliminary conditions of wellbeing.” His proposals for preventing epidemics in prisons urged well ventilated cells and regular washing of inmates, their clothes, and bedding.

Hahnemann devoted as much time to studying chemistry as medicine. And as one contemporary noted, he “would have made a great chemist”—or indeed a pioneering public health doctor, enlightened psychiatrist, or champion of evidence based medicine—“had he not turned out a great quack.”

Sadly his stellar trajectory faltered when he turned to investigating certain treatments by testing them on himself, in time honoured medical tradition, and alighted on cinchona, one of the few effective medicines of the time. Discovered that it produced symptoms similar to those of the ailment it treated—malaria—he vaulted to the conclusion that all effective medicines must show similar symptoms to the disease they cured.

So the principle of treating “like with like” was born and the enduring industry of homoeopathy emerged. Hahnemann expounded his doctrine in his *Organon der rationellen Heilkunde (Organon of Rational Healing)* in 1810. His views excited vociferous opposition and widespread support from the start.

Students attended his lectures in Leipzig only to mock, while the city authorities banned him from practising in 1820. Yet Prince Karl of Schwarzenberg travelled expressly to the area so that Hahnemann could treat him after a stroke. The prince’s death from a second stroke a few months later did nothing to deter continuing patronage from royalty over the ensuing centuries, which helped popularise homoeopathy throughout Europe and especially in England.

Given the fact that homoeopathic remedies were just as likely to work, and much less likely to harm, as the dangerous treatments offered by conventional physicians in Hahnemann’s day, early 19th century patients might be excused their enthusiasm. Later advocates might like to consider Hahnemann’s own creed: “One should proceed as rationally as possible by experiments of the medicines on the human body. Only by these means can the true nature, the real effect, of the medicinal substance be discovered.”

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Grumpy old men

It is generally admitted, wrote R R Madden MD at the beginning of his book *The Infirmities of Genius Illustrated by Referring the Anomalies in the Literary Character to the Constitutional Peculiarities of Men of Genius*, published in 1833, that literary men are an irritable race, subject to many infirmities, both in mind and body. Worldly prosperity and domestic happiness are not often the result of their pursuits.

Fame and frailty, he says, are inseparable companions. This, he continues, is just as well; for it renders those of humbler capacities contented with their lot. Let us “thank God [we] are not like the . . . poor children of genius, frail in health, feeble in resolution, in small matters improvident, and unfortunate in most things.”

Madden was an Irish doctor who served in the tropics, wrote a book of his travels in Turkey and a history of the United Irishmen, and translated *Poems by a Slave in the Island of Cuba, Recently Liberated*, as well as *The History of the Early Life of the Negro Poet, Written by Himself*, published in 1840, when slavery had many years still to run in Cuba.

To what did Dr Madden attribute the irritability of literary men? Unfortunately, like many medical writers of the time, he was not clear or precise in his hypothesising. Most of his examples—Pope, Johnson, Burns, for example—had what he called “dyspepsia,” a protean disorder that accounted for palpitations of the heart, depression of the spirits, and nervous pains in the head.

Most of Madden’s examples had what he called “dyspepsia,” a protean disorder that accounted for palpitations of the heart, depression of the spirits, and nervous pains in the head. This led to “alteration in the structure, softening of its substance, or effusion serous or sanguineous.” We believe something different now: that mental activity preserves the faculties. Where we say, “Use it or lose it,” they said, “Use it and lose it.”

Sixty-one years after Madden published his book about the infirmities of literary men, a scion of the famous Tuke family, J Batty Tuke, delivered the Morison Lectures in Edinburgh entitled “The Insanity of Over-Exertion of the Brain.” (Is it not strange how men with the names Madden and Batty should have been interested in insanity, while Henry Head and Russell Brain became neurologists?)

According to Tuke, over-exertion of the frontal lobes and exhaustion of the neurones by chronic emotion led to Wallerian degeneration. Thus, in treatment, “the first object to be obtained is REST for the brain.” The madman must be put to bed.

Dr Tuke continues, “I need not tell you that the physician is most powerful in the sick-room or hospital, and that he strengthens his position when he orders the patient to bed. Even in cases which at first resist the order, as soon as it is obeyed no difficulty arises in maintaining it. A good nurse, or even two may be necessary.”

We may smile pityingly; but will not our descendants smile at us? Besides, many of my patients asked for help to stop thinking, not any thoughts in particular, but all thoughts whatsoever. They are tired of thought and its responsibilities. I suppose this is one of the reasons that meditation is so popular.

Theodore Dalrymple is a writer and retired doctor

**BETWEEN THE LINES**

**Theodore Dalrymple**

**MEDICAL CLASSICS**

**A Boke or Counsell against the Disease Commonly Called the Sweate or the Sweating Sickness**

By John Caius

First published 1552

Sweating sickness was a disease of unknown cause and very high mortality that first appeared in England in 1485. John Caius’s book is our main source of knowledge about the disease, outbreaks of which occurred until 1578.

John Caius was born in Norwich in 1510. He entered Gonville Hall in Cambridge in 1529 and then moved to Padua to study under Vesalius. He refounded his former college as Gonville and Caius College and became its master. In the first part of his book Caius describes the disease as “not a sweat only (as it is thought or called) but a fever.” It lasted 24 hours, with pain in the arms, legs, back, and shoulders, followed by a “marvellous heavinesse, and a desire to sleepe.”

Dengue fever (“break bone fever”) seems the most likely candidate, although it usually lasts more than 24 hours and is often accompanied by a rash, which the book doesn’t mention. At a time when conditions in England were favourable to the ague (malaria), it is plausible that dengue fever, another mosquito-borne disease, would also be prevalent.

Caius then deals with the causes of the condition: “infection” and “imure spirits in bodies corrupt by repletion (overeating).” Infection is due to “evil misites and exhalations drawn out of the grounde.” Repletion, from eating too much meat, bad meat, or rotten fruit, causes an “excess of humores” to develop.

He then discusses “preservation” (prevention). He recommends a long list of meat, fish, and fruit to eat. In his view people have become effete: “But we are nowe a daies so unwisely fine, and womanly delicate, that we may in no wise touch a fleshe. The olde mannes hardy, stoute courage, & peinfulnes of Englane is utterly driven awaye, in the stede whereof, men now a daies receive womanlines & become nice, not able to withstand a blaste of wynde, or resiste a poore fiseh.”

Caius then goes on to describe “the cure or remedy.” The most important thing is to let out the poison by sweating, he says. He recommends numerous herbs, such as “wilde tansy, mogwort [common wormwood] or feverfew.” Sweating should be provoked by gentle rubbing and warm drinks. The patient’s nose and ears should be put to bed. After 24 hours have passed the patient may get up and put on warm clothes but not go out for two days. Finally, Caius says, “If other causes ther be supernatural, them I leve to the divines to serche, and the diseases thereof to cure, as a matter with out the compassse of my facultie.”

Although Vesalius was beginning to discard Galenical medicine, Caius clearly still clung to Galen’s teaching. Despite sweating being an important symptom of the disease, it is curious that Caius lays great emphasis on the induction of sweating as part of the cure.

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Scott Hitt

Chairied US presidential AIDS council

The full force of AIDS was just beginning to emerge when R Scott Hitt started to practise medicine in 1983 in Los Angeles. The term AIDS was only months old. The first journal article—five rare cases of *Pneumocystis carinii* in young men, all active homosexuals, in Los Angeles—had been published just two years before in *MMWR: Morbidity and Mortality Weekly Report*. The virus itself had yet to be identified and only a few hundred Americans had died from it.

As an openly gay man and physician, at a time when both society and the profession stigmatised homosexuality, Hitt took on the challenges of the epidemic that would decimate his community. With his tall, classic California good looks, intelligence, and winning manner, he quickly became a leader in the medical and political fights against HIV.

He was a member of the Pacific Oaks Medical Group in Beverly Hills, which grew to become one of the largest private HIV medical practices in the country. He served on the governing board of the AIDS Project Los Angeles, a charity that provides social and medical services.

The Reagan administration was slow to respond to the crisis as the death toll mounted into the thousands, then the tens of thousands, a year. Anger rose within the gay community. The pressure group ACT UP emerged and took to the streets with demonstrations.

Hitt took a different tack. He remembered the adage that “money is the mother’s milk of American politics” and set out to change the political dynamic. He was one of the founders of Access Now for Gay and Lesbian Equality (ANGLE) in 1989. The group of Los Angeles powerbrokers included political consultant David Mixner. The group raised prodigious sums from the Hollywood community to advance gay and AIDS issues.

Bill Clinton was governor of Arkansas. His campaign for the Democratic nomination for president was struggling in 1991 when he prepared to speak at the Palace Theater in Hollywood and became the first presidential candidate to speak publicly before a gay crowd.

Hitt would later recount how in the wings of the stage, they told Clinton that half of the audience was HIV positive and would probably be dead within a few years, all in the prime of their lives. The candidate’s eyes went wide. A few minutes later he would say to the audience, “I have a vision and you’re part of it.” He pledged to fight the epidemic. More than 37 000 Americans would die of AIDS that year.

That landmark event opened cheque books and generated volunteer support that contributed to saving Clinton’s political life.

President Clinton created the Presidential Advisory Council on HIV/AIDS (PACHA) in 1995 and named Hitt as its first chairman, at the age of 35, in which capacity he served until 2000. It was the first time that an openly gay man had led a presidential advisory body.

Despair permeated the air when PACHA first met. More than 51 000 Americans would die of the infection that year, the peak of the epidemic, before protease inhibitors miraculously began to ease the affliction. From then on, cadaverous bodies on their death beds began to shed their grey pallor, fill out, and take on a pink glow of health in a resurrection worthy of Lazarus.

As chairman of the council, Hitt faced competing pressures from the gay and AIDS communities and the Clinton administration. Some within the community thought he was simply a good looking fellow who had parleyed his political connections into an appointment; they expected little of him. On the other side, the president was often reluctant to take on controversial aspects of fighting HIV that the council recommended, such as frank prevention messages and support for needle exchange programmes that would reduce transmission among injecting drug users.

Often Hitt was the glue that held the council together. His heart was in the streets but his head realised that too strident an approach would only alienate the president. He sought to craft the council’s recommendations to avoid inflammatory rhetoric and to make them effective. But he never backed down from stating his views.

The issue came to a head in the spring of 1998, when the council, drawing on scientific evidence demonstrating the efficacy of needle exchange programmes in reducing HIV infections without increasing injecting drug use, called for the federal government to fund the programmes.

The president went halfway: he lifted restrictions that prohibited funding the programmes, but he refused to appropriate any money to support them. It is a decision that Clinton, years after leaving office, would acknowledge was wrong. He wished he had had the political courage to do the right thing.

Hitt’s response to the administration’s decision was pointed. “At best this is hypocrisy, at worst, it’s a lie. And no matter what, it’s immoral.” That type of toughness solidified his credibility within the community. Several members of the council resigned in protest, but Hitt felt an obligation to stay and continue to fight for people living with HIV infection.

In 2000 he was the driving force behind creating the American Academy of HIV Medicine, which trains and certifies healthcare workers in treating HIV. He thought it essential that physicians know how to manage the increasingly sophisticated options for treating the disease. And he pressed for state government recognition of the specialty.

Hitt was diagnosed with colon cancer in 1999 and underwent numerous operations and treatment to fight the disease. He leaves his partner of 27 years, Alex Koleszar.

Bob Roehr

Alexis Brook

Former consultant psychiatrist in psychotherapy Tavistock Clinic, London (b 1920; q Cambridge/Middlesex 1943; FRCPsych), died from complications of lymphoma on 7 August 2007. Alexis Brook served with the Royal Army Medical Corps during 1944-7 in India, Burma, and Indo-China and trained in psychiatry at the Maudsley and Napsbury Hospitals, specialising in psychoanalytic psychotherapy at the Cassell Hospital. He established the Tavistock Foundation for funding research and training, and initiated the annual lecture. He was also a senior lecturer at St Bartholomew’s Hospital and consultant in mental health for Islington. After retirement, he continued work in private practice, was honorary consultant psychotherapist at St Mark’s Hospital, and cofounded the Eye and Mind Society developing links with Moorfields Eye Hospital. He leaves a wife, Dite; and three sons.

Sotiris Zalidis

Peter Berman

Former director Stroke Unit, City Hospital, Nottingham (b 1953; q University College Hospital, London, 1976; FRCP), died from cancer of the prostate on 11 August 2007. Soon after his appointment as consultant geriatrician in Nottingham Peter Berman carried out a randomised controlled trial of stroke unit care showing clear benefits on disability and psychological outcomes. Joining the Stroke Unit Trialists’ Collaboration, he contributed to its influential series of systematic reviews. He led the strategic development of stroke services in Nottingham, a beacon of good practice. He was a member of the executive committee of the British Association of Stroke Physicians and served as regional adviser to the Royal College of Physicians. An expert cyclist, during his illness Pete achieved his ambition of climbing Mont Ventoux. He leaves a wife, Ditte, and three sons.

Simon Winner, Stephen Fowlie

William Anthony Jerrett

Former general practitioner Pontyclun, Mid-Glamorgan (b 1934; q Welsh National School of Medicine 1958; OBE, FRCP), died from metastatic prostate cancer on 8 August 2007. After house jobs, William Anthony Jerrett (“Bill”) did national service with the Royal Army Medical Corps in Libya and Cyprus. He was general practitioner in Pontyclun from 1964 to 1994 without a day’s absence through illness. His 1981 paper on lethargy turned out to be the only prospective study on tiredness. He served on the Committee on Safety of Medicines for nine years and was joint course organiser of the local vocational training scheme for ten. After retirement he was chairman of the Mid-Glamorgan Ambulance Trust for four years. He donated the proceeds from his books on medical anecdotes and his last illness to Velindre Hospital Oncology Centre, Cardiff. He leaves a wife, two daughters, and three grandchildren.

Andrew Duffin-Jones

Sally Connellan (née Jerrett)

William Stewart Ogden

Former general practitioner Chalfont St Peter, Buckinghamshire (b 1930; q Cambridge/St Bartholomew’s Hospital, London, 1954; MA), d 11 August 2007. William Stewart Ogden (“Bill”) started his career in ear, nose, and throat surgery at St Bartholomew’s Hospital, London. He spent his two years of national service in the Royal Air Force; in 1957 he moved to Chalfont St Peter to start his lifelong career as a general practitioner. After he retired he spent 12 years as a locum general practitioner in west London. Bill was a founding member of the Chiltern Medical Society, member of the historical section of the Royal Society of Medicine, chairman of the Aspirin Foundation, and consultant to several pharmaceutical companies. He had been a good jazz pianist. He leaves a wife, Barbara, and three children.

David Brodie

John Ogeah

General practitioner London (b 1955; q Ibadan, Nigeria, 1984; BSc, MRCOG, MRCP), died from colon cancer on 23 September 2007. John Ogeah (“Big John”) did a BSc in biochemistry before embarking on a career in medicine. He immigrated to the United Kingdom in 1986 and trained in obstetrics and gynaecology in Ireland. He later retrained in general practice and worked as a general practitioner from 1999 till his death. He was committed to teaching, training, and developing his team, and had a passion for using best evidence. He bore his illness with equanimity reinforced by his strong Catholic faith. He leaves a wife, Benedicta, and two children.

Tubonye C Harry

Margaret Oatway Thorpe

Former general practitioner London (b 1905; q Toronto 1932; DObstRCOg), d 23 June 2007. After qualifying, Margaret Oatway Thorpe moved to England from Canada in 1937. During the second world war she worked at Bethnal Green Hospital, where she met her husband. In 1946 she and her husband set up a joint practice in Hackney, East London, where she specialised in midwifery alongside her work as a general practitioner. She also worked as a medical officer at Holloway women’s prison. After the death of her husband in 1973, Margaret retired from general practice and moved to Hove. She continued to work at Holloway prison and carried out locum duties in Hove until she was almost 80. She had no children but leaves an extended family in Canada. Joan Perren, Dick Perren

Joan Wagstaff

Former general practitioner Hove (b 1914; q University College Hospital, London, 1938), died from heart failure on 9 September 2007. After completing house jobs at University College Hospital, Joan Wagstaff worked in a general practice in Grimsby from 1939 to 1942. She then served in the Royal Army Medical Corps in India from 1942 to 1946. On demobilisation she joined a small general practice in Chingford, where she was very active in the community. In 1967 she moved to a general practice in Hove to help with the care of her ageing parents. She leaves an adopted daughter and three grandchildren.

John Wagstaff
About 1.6 billion mobile phones are in use throughout the world. Along with concerns about exposure to the electromagnetic fields emitted by mobile phone networks are fears that hearing may be damaged by using mobile phones. Thirty young and healthy volunteers with normal hearing had their auditory brainstem responses recorded before and immediately after 10 minutes of genuine or sham exposure to the 900 MHz pulsed electromagnetic field emitted by a commercial mobile phone. The analysis showed no significant differences in the latency of auditory brainstem waves either before or after genuine or sham exposure (BMC Public Health 2007;7:325).

Sociable animals, including humans, need to rapidly recognise friend or enemy within their own species. Now we have evidence that human babies learn how to do this very early in life, before they can talk (Nature 2007;450:557-9). Researchers tested babies aged 6-10 months and were amazed to find that they could distinguish between the helpful or hindering actions of an individual toward a third party. The team speculates that such early engagement in social evaluation may serve as a foundation for moral thought and action later in life.

Exogenous erythropoietin is popular among oncologists to treat the anaemia often induced by chemotherapy. But the use of erythropoiesis stimulating agents is causing some concern to cardiologists and also to the oncologists themselves, who have noticed that in some patients tumours have grown after such agents were used. “Oxygen breathing” may offer an alternative. Renal tissue can be stimulated to patients tumours have grown after such agents were used. “Oxygen breathing” may offer an alternative. Renal tissue can be stimulated to

Is acute appendicitis being overdiagnosed? Yes, especially in women, say surgeons in the Annals of the Royal College of Surgeons of England (2007;89:766-9). Histological confirmation of appendicitis was established in just 52% of women who had their appendix taken out, compared with 81% in men. Among the normal looking appendixes taken from women, several showed fibro-obliterative changes, luminal inflammation, serositis, and faecoliths, and

one even had pinworm. In women at least, say the authors, diagnostic laparoscopy should be performed before appendicectomy.

Patients given total parenteral nutrition are at high risk of bloodstream infections. Intravenous energy intake and glucose are thought to lead to hyperglycaemia, which in turn leads to bloodstream infection. To test this idea, researchers analysed 200 consecutive patients who were started on total parenteral nutrition during one year. Increased energy intake, but not hyperglycaemia, was confirmed as an independent risk factor for bloodstream infections. The authors say that even short periods of increased energy intake should be avoided (Critical Care 2007;11:R114).

We’re familiar with hip and knee replacements, but what about shoulders? End stage arthritis of the shoulder causes great pain and disability, especially in older people, and shoulder arthroplasty offers the chance of considerable improvement in function and the ability to remain independent. In one unit, 14% of shoulder replacement operations were performed in people over 80 and resulted in minimal morbidity and rapid rehabilitation (Journal of Bone and Joint Surgery 2007;89-B:1466-9).

Three cities in France took part in a cohort study to find out if diet contributes to the risk of developing dementia (Neurology 2007;69:1921-30). Daily consumption of fruit and vegetables was associated with a decreased risk of all causes of dementia, and a weekly consumption of fish was associated with a reduced risk of Alzheimer’s disease, but only in people who were not carriers of the ε4 allele of ApoE. Regular consumption of omega-6 rich oils but not omega-3 rich oils or fish was associated with an increased risk of dementia among people who did not carry the allele.

Paroxysmal nocturnal haemoglobinuria puts patients at high risk of venous thrombosis, and once that happens, even when patients are given anticoagulants, the problem tends to progress and recur. Something better is needed—and a study in Blood (2007;110:4123-8) could have the answer. Eculizumab, an antibody to complement C5, seems to greatly inhibit thrombosis in affected patients. With treatment the thromboembolic event rate was 1.07 per 100 patient years, compared with 7.37 events per 100 patient years before eculizumab—a reduction of 85%.

Poorer countries need to identify cheap sources of dietary iron to tackle iron deficiency and anaemia. One possibility is seaweed. A study in the Journal of Nutrition (2007;137:2691-5) analysed the bioavailability from four species of algae included in a rice based meal. The highest iron concentrations were found in Sargassum, with Gracilariaopsis, Ulva, and Porphyra as runners-up. Cooking the algae didn’t seem to affect the absorption of iron.