

Deciding who to admit to a critical care unit

Eddy Fan and Dale M Needham

BMJ 2007;335;1103-1104; originally published online 1 Nov 2007; doi:10.1136/bmj.39378.654329.80

Updated information and services can be found at: http://bmj.com/cgi/content/full/335/7630/1103

These	incl	lude
111000	11101	uue.

References	This article cites 10 articles, 3 of which can be accessed free at: http://bmj.com/cgi/content/full/335/7630/1103#BIBL
	1 online articles that cite this article can be accessed at: http://bmj.com/cgi/content/full/335/7630/1103#otherarticles
Rapid responses	2 rapid responses have been posted to this article, which you can access for free at: http://bmj.com/cgi/content/full/335/7630/1103#responses
	You can respond to this article at: http://bmj.com/cgi/eletter-submit/335/7630/1103
Email alerting service	Receive free email alerts when new articles cite this article - sign up in the box at the top left of the article

Notes

To order reprints follow the "Request Permissions" link in the navigation box

Editorials represent the opinions of the authors and not necessarily those of the *BMJ* or BMA

EDITORIALS

For the full versions of these articles see bmj.com

Deciding who to admit to a critical care unit

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



RESEARCH, p 1132

Eddy Fan instructor Dale M Needham assistant

professor, Johns Hopkins Medical Institutions, Division of Pulmonary and Critical Care Medicine, Baltimore, MD 21205, USA dale.needham@jhmi.edu Competing interests: None declared.

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

BMJ 2007;335:1103-4

doi: 10.1136/bmj.39378.654329.80

This article was published on bmj.com on 1 November 2007

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 2030.¹ 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.² 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.³ ⁴

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,³ previous studies have also shown significant variability in doctors' estimates of survival for people with an exacerbation of COPD who need mechanical ventilation.^{5 6}

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.⁷ Quality of life after intensive care is an important consideration also,⁸ especially as-for instancenearly 90% of seriously ill people would rather die than survive with severe cognitive impairment.⁹ 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.² Like predicting patient mortality, the ability of doctors and nurses to predict quality of life after intensive care is unsatisfactory.¹⁰

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.11 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.¹² 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.

- World Health Organization. Chronic obstructive pulmonary disease (COPD): burden. 2007. www.who.int/respiratory/copd/ burden/en/index.html.
- Wildman MJ, Sanderson C, Groves J, Reeves BC, Ayres J, Harrison D, et al. Prognostic pessimism for patients with chronic obstructive pulmonary disease (COPD) or asthma admitted to intensive care in the UK: multicentre observational cohort study. *BMJ* 2007 doi: 10.1136/bmj.39371.524271.55.
- 3 Connors AF Jr, Dawson NV, Thomas C, Harrell FE Jr, Desbiens N, Fulkerson WJ, et al. Outcomes following acute exacerbations of severe chronic obstructive lung disease. Am J Respir Crit Care Med 1996;154:959-67.

Downloaded from bmj.com on 19 July 2008

- Gupta D, Keogh B, Chung KF, Ayres JG, Harrison DA, Goldfrad C, et al. Characteristics and outcome for admissions to adult, general critical care units with acute severe asthma: a secondary analysis of the ICNARC case mix programme database. *Crit Care* 2004;8:R112-21.
- 5 Pearlman RA. Variability in physician estimates of survival for acute respiratory failure in chronic obstructive lung disease. *Chest* 1987;91:515-21.
- 6 Wildman M, O'Dea J, Kostopolou O, Tindall M, Walia S, Khan Z. Variation in intubations decisions for patients with chronic obstructive pulmonary disease in one critical care network. QJ Med 2003;96:583-91.
- 7 The SUPPORT Principal Investigators. A controlled trial to improve care for seriously ill hospitalized patients: the study to understand prognoses and preferences for outcomes and risks of treatments (SUPPORT). JAMA 1995;273;1591-8.
- 8 Dowdy DW, Eid MP, Sedrakyan A, Mendez-Tellez PA, Pronovost

PJ, Herridge MS, et al. Quality of life in adult survivors of critical illness: a systematic review of the literature. *Intensive Care Med* 2005;31:611-20.

- 9 Fried TR, Bradley EH, Towle VR, Allore H. Understanding the treatment preferences of seriously ill patients. N Engl J Med 2002;346:1061-6.
- 10 Frick S, Uehlinger DE, Zuercher Zenklusen RM. Medical futility: predicting outcome of intensive care unit patients by nurses and doctors—a prospective comparative study. *Crit Care Med* 2003;31:456-61.
- 11 Vincent JL. Forgoing life support in western European intensive care units: the results of an ethical questionnaire. *Crit Care Med* 1999;27:1626-33.
- 12 Rapoport J, Teres D, Barnett R, Jacobs P, Shustack A, Lemeshow S, et al. A comparison of intensive care utilization in Alberta and western Massachusetts. *Crit Care Med* 1995;23:1336-46.

Doctors and climate change Health professionals have a duty to be part of the solution

LETTERS, p 1110 NEWS, p 1116

Mike Gill retired south east regional chair of public health, London NW6 4DG Fiona Godlee editor in chief, *BMJ*, London WC1H 9JR Richard Horton editor in chief, *Lancet*, London NW1 7BY Robin Stott vice chair, Medact, London N1 6HT stott@dircon.co.uk

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. Provenance and peer reviewe. Commissioned; not peer reviewed.

BMJ 2007;335:1104-5 doi:10.1136/bmj.39412.488021.80 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."¹ 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.²



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.^{3 4}

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,⁵ ⁶ 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.7-9 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.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.

- 1 General Medical Council. Good medical practice. 2006. www.gmcuk.org/guidance/good_medical_practice/index.asp.
- 2 Alvarez W. *Tyrannosaurus rex and the crater of doom*. Princeton, NJ: Princeton University Press, 2007.
- 3 HM Treasury. Stern review final report. 2006. www.hm-treasury.gov. uk/independent_reviews/stern_review_economics_climate_ change/sternreview_index.cfm.
- 4 Intergovernmental Panel on Climate Change. Working Group III Climate Change. Mitigation of Climate Change. Summary for policy makers. 2007. http://195.70.10.65/pdf/assessment-report/ar4/ wg3/ar4-wg3-spm.pdf.
- 5 Roberts I. When doctors learned to speak carbon. BMJ 2006;332:497.
- 6 Stott R, Godlee F. What shall we do about climate change? BMJ 2006;333:983-4.
- Stott R. Healthy response to climate change. *BMJ* 2006;332:1385-7.
 Horton R. Righting the balance: energy and health. *Lancet*
- 2007;370:921.
 9 Energy and Health Supplement. *Lancet* 2007. Published online 13 September 2007.
- 10 Global Commons Institute. *Contraction and convergence*. A global solution to a global problem. 2006. www.gci.org.uk.

Screening for prostate cancer in younger men Clinicians should promote informed decision making while awaiting definitive evidence from RCTs

RESEARCH, p 1139

Dragan Ilic senior lecturer Sally Green professor, of Health Services Research, Monash University, Locked Bag 29, Monash Medical Centre, Clayton VIC 3168, Australia dragan.ilic@med.monash.edu.au

Competing interests: SG is the director of the Australasian Cochrane Centre and a member of the Cochrane Collaboration steering committee. DI and SG have received funding from Andrology Australia, which is a community and professional education programme funded by the Australian government that provides health information on male reproductive health.

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

BMJ 2007;335:1105-6 doi: 10.1136/bmj.39385.491424.80

This article was published on bmj.com on 15 November 2007

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.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).²

A recent systematic review¹ identified two randomised controlled trials (RCTs) assessing the effectiveness of screening for prostate cancer.^{3 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.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. 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.⁸ These factors may all increase conflict in making decisions or uncertainty associated with treatment.⁸ 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.⁹

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.

- 1 Ilic D, O'Connor D, Green S, Wilt T. Screening for prostate cancer. Cochrane Database Syst Rev 2006;(3):CD004720.
- 2 Lane J, Howson J, Donovan J, Goepel J, Dedman D, Down L, et al. Detection of prostate cancer in unselected young men: prospective cohort nested within a randomised controlled trial. *BMJ* 2007, doi: 10.1136/bmj.39381.436829.BE.
- 3 Labrie F, Candas B, Cusan L, Gomez J, Bélanger A, Brousseau G, et al. Screening decreases prostate cancer mortality: 11-year follow-up of the1988 Quebec prospective randomized controlled trial. *Prostate* 2004;59:311-8.
- 4 Sandblom G, Varenhorst E, Lofman O, Rosell J, Carlsson P. Clinical consequences of screening for prostate cancer: 15 years follow-up of a randomised controlled trial in Sweden. *Eur Urol* 2004;46:717-24.
- 5 Schroder F, Denis L, Roobol M, Nelen V, Auvinen A, Tammela T, et al; ERSPC. The story of the European randomized study of screening for prostate cancer. *BJU Int* 2003;92:1-13.
- Prorok P, Andriole G, Bresalier R, Buys S, Chia D, Crawford D, et al. Design of the prostate, lung, colorectal and ovarian (PLCO) cancer screening trial. *Control Clin Trials* 2000;21:273S-309S.
- 7 Donovan J, Hamdy F, Neal D, Peters T, Oliver S, Brindle L, et al. Prostate test for cancer and treatment (ProtecT) feasibility study. *Health Technol Assess* 2003;74:88.
- 8 Ilic D, Risbridger G, Green S. The informed man: attitudes and information needs on prostate cancer screening. J Mens Health Gend 2005;2:414-20.
- O'Connor AM, Stacey D, Entwistle V, Llewellyn-Thomas H, Rovner D, Holmes-Rovner M, et al. Decision aids for people facing health treatment or screening decisions. *Cochrane Database Syst Rev* 2003;(1):CD001431.

Communicating risk to the public after radiological incidents

Providing detailed, comprehensible, and relevant health information is essential

RESEARCH, p 1143

Steven M Becker associate professor of public health and vice chair, Department of Environmental Health Sciences, University of Alabama at Birmingham, Birmingham, AL 35294, USA smbecker@uab.edu

Competing interests: None declared.

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

BMJ 2007;335:1106-7

doi: 10.1136/bmj.39377.655845.80

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 2006.¹ 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.²

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 150 000 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 112 000 people sought radiological monitoring in special facilities.^{7 8} 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 2000.⁹

The above experience relates to accidents involving

This article was published on bmj.com on 1 November 2007

radioactive materials. But since the terrorist attacks in New York and London, many people involved in emergency preparedness are worried about how the public might react to a large scale intentional release of radioactive materials. This question is difficult to answer. Few malicious releases have ever been recorded, and opportunities for systematic study have been rare. Thus, researchers have relied largely on simulations, hypothetical scenarios, and extrapolations from experience with accidents to try to understand people's views and information needs. That is why the study by Rubin and colleagues is so important. The study uses extensive data gathered during the 2006 polonium incident and helps us to understand perceptions, reactions, and risk communication strategies during a real world incident involving the intentional release of radioactive materials.

One of the study's most interesting findings is that only 11% of the 1000 Londoners surveyed perceived their health to be at risk from the incident. The authors suggest two explanations for this. Firstly, most of those surveyed did not view the incident as terrorism or a public health threat. Rather, it was seen as a criminal act or an act of espionage. Likewise, the act was seen as being targeted at one, or perhaps a few, specific people, rather than being targeted at the public.

Secondly, nearly three quarters of respondents agreed with the statement that, "if you have not been in one of the areas known to be contaminated with polonium 210, then there is no risk to your health." This was one of the key messages of the public information campaign undertaken by health agencies, and the findings suggest that those efforts were successful. In short, the relatively low levels of health concern about the incident seem to have resulted from the way that people categorised the incident and from effective risk communication.

What are the broader implications for preparedness

and response? As the authors rightly point out, things could have unfolded differently if more people had perceived the event as related to terrorism. According to the survey results, the minority of people who did perceive it in this way were more likely to believe their health was at risk. This suggests that in a large scale terrorist attack involving radioactive materials (for example, a "dirty bomb"), levels of public concern could be dramatically higher.

This should only serve to emphasise what Rubin and colleagues conclude—that it is essential to give the public access to detailed, comprehensible, and relevant health information. Indeed, in a terrorist incident involving radioactive materials, effective risk communication may be the most important way to reduce morbidity and mortality, tackle people's concerns, avoid the impact on behaviour, and maintain public trust and confidence. As such, improved crisis and emergency risk communication needs to be at the heart of future planning and training.

- Rubin GJ, Page L, Morgan O, Pinder RJ, Riley P, Hatch S, et al. Public information needs after the poisoning of Alexander Litvinenko with polonium-210 in London: cross sectional telephone survey and qualitative analysis. *BMJ* 2007 doi: 10.1136/bmj.39367.455243.BE.
- 2 National Council on Radiation Protection and Measurements. Management of terrorist events involving radioactive material. NCRP report number 138. Bethesda, MD: NCRP, 2001.
- Slovic P, ed. The perception of risk. London: Earthscan Publications, 2001.
 Becker SM. Emergency communication and information issues in terrorism events involving radioactive materials. *Biosecur Bioterror* 2004;2:195-207.
- 5 Becker SM. Addressing the psychosocial and communication challenges posed by radiological/nuclear terrorism: key developments since NCRP 138. *Health Phys* 2005:89:521-30.
- 6 Erikson K. A new species of trouble: the human experience of modern disasters. New York: WW Norton, 1994.
- 7 Collins DL, de Carvalho AB. Chronic stress from the Goiania 137Cs radiation accident. *Behav Med* 1993:18:149-57.
- International Atomic Energy Agency. The radiological accident in Goiania, STI/PUB/815. Vienna: IAEA, 1988.
 Backer SM, Pserkosocial effects of radiation accidents. In: Gusen
- Becker SM. Psychosocial effects of radiation accidents. In: Gusev I, Guskova A, Mettler FA Jr, eds. *Medical management of radiation accidents*, 2nd ed. Boca Raton: CRC Press, 2001:519-25.

Obesity and cancer

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

RESEARCH, p 1134

Eugenia E Calle managing director of analytic epidemiology, American Cancer Society, Atlanta, GA 30303, USA jeanne.calle@cancer.org

Competing interests: None declared. Provenance and peer review: Commissioned; not externally peer reviewed.

BMJ 2007;335:1107-8 doi: 10.1136/bmj.39384.472072.80

This article was published on bmj.com on 6 November 2007 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. Increasing BMI was associated with significantly increased incidence of postmenopausal breast cancer, endometrial cancer, kidney cancer, and adenocarcinoma of

Downloaded from bmj.com on 19 July 2008



RIAN HARRIS/

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.³⁻⁷ 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 2.0.3 4 8 9 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.¹⁰ 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.11 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 cancer⁴ ¹² 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.³ The worldwide obesity epidemic shows no signs of abating, so insight 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.

- Reeves GK, Pirie K, Beral V, Green J, Spencer E, Bull D; for the Million Women Study Collaborators. Cancer incidence and mortality in relation to body mass index in the million women study: cohort study. BMJ 2007 doi: 10.1136/bmj.39367.495995.AE.
- 2 International Agency for Research on Cancer. IARC handbooks of cancer prevention. Weight control and physical activity. Lyon: IARC, 2002.
- 3 Calle EE, Kaaks R. Overweight, obesity and cancer: epidemiological
- evidence and proposed mechanisms. Nat Rev Cancer 2004;4:579-91.
 Calle EE. Adiposity and cancer. In: Fantuzzi G, Mazzone T, eds. Nutrition and health: adipose tissue and adipokines in health and disease. Totowa, NJ: Humana Press, 2007:307-25.
- 5 Kasim K, Levallois P, Abdous B, Auger P, Johnson KC. Lifestyle factors and the risk of adult leukemia in Canada. *Cancer Causes Control* 2005;16:489-500.
- 6 Chiu BC, Gapstur SM, Greenland P, Wang R, Dyer A. Body mass index, abnormal glucose metabolism, and mortality from hematopoietic cancer. *Cancer Epidemiol Biomarkers Prev* 2006;15:2348-54.
- 7 Bosetti C, Negri É, Gallus S, Dal Maso L, Franceschi S, La Vecchia C. Anthropometry and multiple myeloma. *Epidemiology* 2006;17:340-1.
- 8 Samanic C, Chow WH, Gridley G, Jarvholm B, Fraumeni JF Jr. Relation of body mass index to cancer risk in 362,552 Swedish men. *Cancer Causes Control* 2006;17:901-9.
- 9 Larsson SC, Permert J, Hakansson N, Naslund I, Bergkvist L, Wolk A. Overall obesity, abdominal adiposity, diabetes and cigarette smoking in relation to the risk of pancreatic cancer in two Swedish populationbased cohorts. *Br J Cancer* 2005;93:1310-5.
- Stolzenberg-Solomon R, Graubard B, Chari S, Limburg P, Taylor P, Virtamo J, et al. Insulin, glucose, insulin resistance, and pancreatic cancer in male smokers. *JAMA* 2005;294:2872-8.
 Patel AV, Rodriguez C, Bernstein L, Chao A, Thun MJ, Calle EE. Obesity,
- 11 Patel AV, Rodriguez C, Bernstein L, Chao A, Thun MJ, Calle EE. Obesity, recreational physical activity, and risk of pancreatic cancer in a large US cohort. *Cancer Epidemiol Biomarkers Prev* 2005;14:459-66.
- 12 Pischon T, Lahmann PH, Boeing H, Friedenreich C, Norat T, Tjonneland A, et al. Body size and risk of colon and rectal cancer in the European prospective investigation into cancer and nutrition (EPIC). J Natl Cancer Inst 2006;98:920-31.