



bmj.com To submit a rapid response go to any article on bmj.com and click “respond to this article”

LETTERS

UK CANCER SURVIVAL STATISTICS

Survival is multifactorial

Beral and Peto’s assessment of cancer registration in the United Kingdom does not reflect recent practice.¹ In Scotland data are gathered from multiple sources, including pathology reports. Typically, most (>95%) breast cancers are recorded as microscopically verified, around 0.1% are “notified” solely by death record, and <0.5% end up as “death certificate only” registrations. By referring to source documents, staff make every effort to capture the earliest available date of diagnosis and avoid registering recurrences. Ascertainment of breast cancer in Scotland was estimated to exceed 98% compared with five clinical trials databases comprising 2621 patients and spanning the period of diagnosis 1978–2000.²

The UK’s reported relative survival for a few types of cancer exceeds the notional “European average.”³ This is not consistent with a systematic artefact of data processing that might be expected to operate in the

same direction across all cancers. We remain unconvinced that differences in data quality are substantial enough to explain the survival differences observed between the UK and the Nordic countries (except Denmark, which like its neighbours has statutory cancer registration yet reports survival rates similar to those in the UK for several major cancers).³

Data quality is only one of many potential explanations for differences in survival from cancer observed between countries (box).⁴ Despite the welcome decrease in breast cancer mortality since the late 1980s, it remains comparatively high. It would be unfortunate if policymakers were to conclude that the recent investment in cancer services might have been unnecessary on the basis of somewhat insecure international comparisons of mortality trends alone.⁵

David H Brewster director, Scottish Cancer Registry,
David.Brewster@nhs.net

Roger J Black head, Cancer Information Programme,
Information Services Division, NHS National Services
Scotland, Edinburgh EH12 9EB

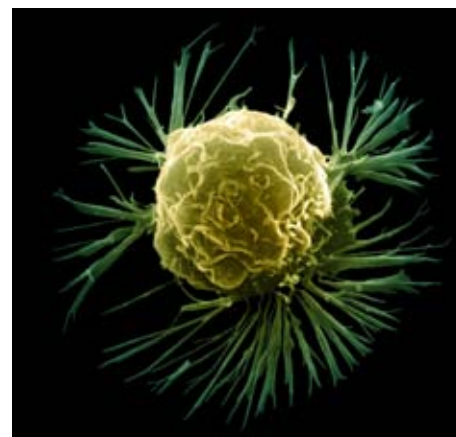
Competing interests: None declared.

- 1 Beral V, Peto R. UK cancer survival statistics. *BMJ* 2010;341:c4112. (14 August.)
- 2 Brewster DH, Stockton DL. Ascertainment of breast cancer by the Scottish Cancer Registry: an assessment based on comparison with five independent breast cancer trials databases. *Breast* 2008;17:106–8.
- 3 Sant M, Allemani C, Santaquilani M, Knijn A, Marchesi F, Capocaccia R; EUROCARE Working Group. EUROCARE-4. Survival of cancer patients diagnosed in 1995–1999. Results and commentary. *Eur J Cancer* 2009;45:931–91.
- 4 Black RJ, Sankaranarayanan R, Parkin DM. Interpretation of population-based cancer survival data. In: Sankaranarayanan R, Black RJ, Parkin DM, eds. *Cancer survival in developing countries*. International Agency for Research on Cancer, 1998. (IARC scientific publications No 145.)
- 5 Brewster DH, Black RJ. It is more informative to examine mortality alongside incidence and survival. Rapid response. bmj.com 2010. www.bmj.com/content/341/bmj.c4112.full/reply#bmj_el_240264.

Cite this as: *BMJ* 2010;341:c5133

Reflect NHS clinical realities

Beral and Peto argue that the British and Irish cancer registries’ consistent record of inferior survival compared with other European countries is caused by survival estimation biased by incomplete registration.¹ However, poor survival from lung cancer in the UK compared with Italy has been confirmed using prospectively acquired data rather than



SCIENCE SOURCE/SPL

registration records,² and “death certificate only” registrations are not randomly distributed among the population but are related to reduced access to diagnosis and treatment.³

The comparatively poor survival of British patients with lung and other cancers is associated with more advanced stage at presentation.² This factor is shared with Denmark, another European country with comparatively poor survival.⁴ In both countries patients are obliged to access specialist services through primary care. All who treat cancer are familiar with patients who have received treatment for ambiguous symptoms for some time. General practitioners see many indistinguishable patients whom they manage successfully without incurring the costs of referral and investigation because they do not have cancer. We must explore the effect of the contradictory functions we ask of GPs—to be diagnostician and gatekeeper.

The excellence of secondary and tertiary institutions cannot restore the survival prospects of a patient who attends a GP with symptoms that were due to curable early cancer but has incurable metastatic disease by the time the diagnosis comes to light. We are now learning how much traffic in primary care is generated during the time leading up to the diagnosis of cancer.⁵

S Michael Crawford consultant medical oncologist, Airedale General Hospital, Keighley, West Yorkshire BD20 6TD
michael.crawford@anhst.nhs.uk

Competing interests: None declared.

- 1 Beral V, Peto R. UK cancer survival statistics. *BMJ* 2010;341:c4112. (14 August.)
- 2 Imperatori A, Harrison RN, Leitch DN, Rovera F, Lepore G, Dionigi G, et al. Lung cancer in Teesside (UK) and Varese (Italy): a comparison of management and survival. *Thorax* 2006;61:232–9.
- 3 Jones AP, Haynes R, Sauerzapf V, Crawford SM, Forman D. Geographical access to healthcare in Northern

Factors affecting survival from cancer⁴

Quality of data

Population coverage
Completeness of ascertainment
Accuracy of registration
Completeness of follow-up
“Death certificate only” registrations

The host

Age
Sex
Socioeconomic position
Race and ethnic group
Comorbidity
Mortality from other causes
Behaviour

The tumour

Extent of disease
Site (and sub-site)
Morphology
Biology

Health care

Screening
Diagnostic facilities
Treatment facilities
Quality of treatment
Follow-up care

England and post-mortem diagnosis of cancer. *J Pub Health* 2010; doi: 10.1093/pubmed/fdq017.

4 Olesen F, Hansen RP, Vedsted P. Delay in diagnosis: the experience in Denmark. *Br J Cancer* 2009;101:S5-8.

5 Hamilton W. The CAPER studies: five case-control studies aimed at identifying and quantifying the risk of cancer in symptomatic primary care patients. *Br J Cancer* 2009;101:S80-6.

Cite this as: *BMJ* 2010;341:c5134

Editor's note: The authors of the editorial say they are too busy to reply at present but will do so in due course.

POST-PUBLICATION REVIEW

A tale of woe

Schriger and Altman show that post-publication review of medical research is inadequate.¹

Some years ago a high impact specialty journal published the results of a randomised controlled trial that I thought was flawed in its methods and data interpretation. I submitted a letter with my comments through the approved channel. Neither the letter nor a follow-up enquiry was acknowledged. My letter was never published.

A few months later a further paper based on the same trial was published in a lower impact, more specialist journal. My letter was published this time, but the authors did not respond.

When the results of the study were used to market the seemingly more effective technology I again questioned the results with a local sales representative of the manufacturer, who said he would make enquiries. I heard nothing. The manufacturer is a large international company, which not only sponsored the trial but also is a major financial backer of the annual conference of the professional society that publishes the first journal I wrote to.

As a clinical researcher, systematic reviewer, and guideline developer I value post-publication criticism and debate. Could a condition of publication be an obligation to respond to criticism?

Fergus R Macbeth director, Centre for Clinical Practice, National Institute for Health and Clinical Excellence, London WC1V 6NA
fergus.macbeth@nice.org.uk

Competing interests: None declared.

1 Schriger DL, Altman DG. Inadequate post-publication review of medical research. *BMJ* 2010;341:c3803. (11 August.)

Cite this as: *BMJ* 2010;341:c5147

Embrace the “market of ideas”

Schriger and Altman bemoan the inadequacy of post-publication review,¹ but surely they have too limited a concept of post-publication review. They don't explicitly define post-publication review, but they imply that it is the

process of people writing to criticise published reports and the authors responding. This is much too narrow a view and is making the common mistake of confusing the publishing of science with its doing.

I would define post-publication review as the process whereby scientists and others decide whether a piece of work matters. I suggest that this doesn't happen much through debate in the correspondence pages of journals, but rather through scientists and other consumers of research recommending others to pay attention to a piece of research, conducting other studies off the back of it, absorbing it into systematic reviews, beginning to act on its conclusions, throwing it in the bin, and taking a thousand other actions that constitute the “market of ideas.”

Why waste your time writing to journals, particularly when, as Schriger and Altman imply, “many research studies don't matter much and most don't matter at all”?

Richard Smith professional loudmouth, Clapham
richardswsmith@yahoo.co.uk

Competing interests: RS is a former editor of the *BMJ*, a friend of Doug Altman, on the board of the Public Library of Science, and increasingly convinced that the processes of publishing science are broken.

1 Schriger DL, Altman DG. Inadequate post-publication review of medical research. *BMJ* 2010;341:c3803. (11 August.)

Cite this as: *BMJ* 2010;341:c5148

LOST WITHOUT TRANSLATION

EC's science-friendly future

Watts describes research funders' increasing emphasis on translational research and cites the European Commission's seventh framework programme as an example.¹ On 19 July 2010 my colleagues and I announced the publication of our 2011 work programme and its corresponding calls for research proposals. The work programme has a budget of €681m and spans the continuum from basic to translational research. The deadlines for submitting proposals through the online application system are 13 October and 20 November 2010, dependent on application type.

Eight of the 51 topics aim at supporting clinical trials to verify the safety and efficacy of various treatments and to promote the translation of research into clinical practice, each

of which may result in several projects receiving up to €6m. Successful projects will target results increasing therapeutic options for patients and stimulate the implementation of best practice in member states. Topics address issues as diverse as regenerative medicine, brain related diseases, human development and ageing, antimicrobial drug resistance, cancer, cardiovascular diseases, diabetes and obesity, and off-patent medicines for children.

Ten further topics require that at least 15% or 30% of the EU grant is allocated to small and medium sized enterprises. Two of them will support ambitious high impact research initiatives in immunisation and in epi-genomics with up to €30m of EU funding.

More information is available at <http://cordis.europa.eu/fp7/health/>

Ruxandra Draghia-Akli director, health research, Research Directorate General—European Commission, B-1049 Brussels, Belgium
Ruxandra.Draghia-Akli@ec.europa.eu

Competing interests: None declared.

1 Watts G. Lost without translation? *BMJ* 2010;341:c4363. (18 August.)

Cite this as: *BMJ* 2010;341:c5016

HYPERTENSION OF PREGNANCY

Why no calcium?

Guidance on hypertensive disorders of pregnancy from the National Institute for Health and Clinical Excellence (NICE) says that evidence for the preventive effect of calcium supplementation is “conflicting and confusing.”¹ A cynic might say that this was a handy conclusion if your department's future funding depends on lush grants for further randomised trials.

Perhaps the brains behind the NICE report simply believe it their duty to hold back our impulsiveness, and stop us from rushing in to supplement calcium after only five decades or so of trials.

What is conflicting and confusing about these facts?

- Good biochemical reasons explain why calcium supplementation should help to prevent pre-eclampsia
- Cochrane says that it halves the problem²
- It is safe and cheap
- Diet cannot give the required amounts (equivalent to 1 l milk daily)
- Dietary inadequacy is common
- It makes giving vitamin D easy.

Of course questions remain—for example, dose and screening for hypercalcaemia. It also works best in those who are most deficient, and not everyone benefits.

Alongside the translational research revolution,³ we need a new lexicon in writing conclusions to analyses. Rather than saying, “benefit uncertain . . . more randomised trials



needed . . . can't recommend," we need a new boldness: "This seems to work, but we don't know the dose, or whether everyone should get it, or for what duration, or whether there may be long term issues."

Laurence Wood obstetrician, University Hospitals Coventry and Warwickshire NHS Trust laurence.wood@uhcw.nhs.uk

Competing interests: None declared.

- 1 Visintin C, Muggleston MA, Almerie MQ, Nherera LM, James D, Walkinshaw S, on behalf of the Guideline Development Group. Management of hypertensive disorders during pregnancy: summary of NICE guidance. *BMJ* 2010;341:c2207. (25 August.)
- 2 Hofmeyr GJ, Atallah AN, Duley L. Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems. *Cochrane Database Syst Rev* 2006 Issue 4 (ISSN 1464-780X).
- 3 Watts G. Lost without translation. *BMJ* 2010;341:c4363. (18 August.)

Cite this as: *BMJ* 2010;341:c5167

Why no magnesium sulphate?

The management of pre-eclampsia with severe hypertension in the guidance from the National Institute for Health and Clinical Excellence (NICE)¹ may seem too conservative for clinicians who have observed maternal eclampsia, cerebral haemorrhage, liver haematoma, abruptio placentae, or fetal death. I could not find any reference to prophylactic treatment with magnesium sulphate in the summary, although it reduces the risk of eclampsia and maternal death.²

Olivier Irion director, Department of Obstetrics and Gynaecology, University of Geneva, University Hospitals of Geneva, CH 1211 Geneva, Switzerland olivier.irion@hcuge.ch

Competing interests: None declared.

- 1 Visintin C, Muggleston MA, Almerie MQ, Nherera LM, James D, Walkinshaw S, on behalf of the Guideline Development Group. Management of hypertensive disorders during pregnancy: summary of NICE guidance. *BMJ* 2010;341:c2207. (25 August.)
- 2 Altman D, Carroli G, Duley L, Farrell B, Moodley J, Neilson J, et al; Magpie Trial Collaboration Group. Do women with pre-eclampsia, and their babies, benefit from magnesium sulphate? The Magpie Trial: a randomised placebo-controlled trial. *Lancet* 2002;359:1877-90.

Cite this as: *BMJ* 2010;341:c5165

NICE ON CHRONIC HEART FAILURE

What about access to investigations?

The updated guidance from the National Institute for Health and Clinical Excellence (NICE) on chronic heart failure in adults recommends that serum natriuretic peptides (B-type natriuretic peptide or N-terminal pro-B-type natriuretic peptide) should be measured in patients with suspected heart failure without previous myocardial infarction.¹ Similarly the latest NICE guidance on chest pain of recent onset



recommends computed tomography and measurement of calcium score for those with a 10-29% likelihood of coronary artery disease. For those with a likelihood of 30-60% it recommends non-invasive functional imaging with either myocardial perfusion scintigraphy with single photon emission computed tomography, stress echocardiography, and first pass contrast enhanced magnetic resonance perfusion or magnetic resonance imaging for stress induced wall motion abnormalities as the most cost effective investigation.

These investigations are currently not routinely available in my area. In particular, general practitioners have no access to serum natriuretic peptide measurement. Exercise electrocardiography seems to be still widely used to confirm the diagnosis or assess whether patients should have angiography. If guidelines are to mean anything, access is needed to the recommended investigations.

Donald Macaulay general practitioner, Blackburn Health Centre, West Lothian drdmacaulay@hotmail.com

Competing interests: None declared.

- 1 Al-Mohammad A, Mant J, Laramie P, Swain S, on behalf of the Chronic Heart Failure Guideline Development Group. Diagnosis and management of adults with chronic heart failure: summary of updated NICE guidance. *BMJ* 2010;341:c4130. (25 August.)

Cite this as: *BMJ* 2010;341:c5010

DECISIONS IN DEMENTIA

Carers are central

Respondents to a public consultation of the Nuffield Council on Bioethics on the ethics of dementia raised the same problems and dilemmas as identified by Livingston and colleagues.¹ We also heard from carers that professionals seemed to treat them with suspicion and that information that would be useful in their

caring role was not provided because of concerns about confidentiality.

The resulting report looks at the journey of the person with dementia and their carer(s) from pre-diagnosis onwards.² Its ethical framework supports paid and unpaid carers in decision making, recognising that people rarely make decisions in isolation, and that autonomy can be promoted in people with dementia by encouraging relationships that are important to them. The codes of practice for current UK mental capacity legislation should be amended to promote this concept, and appropriate training and support be available for all carers.

The report also points out that the capacity of a person with dementia to make decisions is not all or nothing. Capacity may vary considerably in relation to the same decision: people often have good and bad times of the day, and cognitive abilities may also be affected by factors unconnected with their dementia, such as other illnesses or emotional wellbeing.

The respondents to the public consultation emphasised the importance of information, support, and access to services after diagnosis. Fact sheets for carers on decision making, such as those produced by Livingston and colleagues, should be made widely available.

Hugh Whittall director, Nuffield Council on Bioethics, London WC1B 3JS hwhittall@nuffieldbioethics.org

Competing interests: None declared.

- 1 Livingston G, Leavey G, Manela M, Livingston D, Rait G, Sampson E, et al. Making decisions for people with dementia who lack capacity: qualitative study of family carers in UK. *BMJ* 2010;341:c4184. (18 August.)
- 2 Nuffield Council on Bioethics. Dementia: ethical issues. 2009. www.nuffieldbioethics.org/dementia.

Cite this as: *BMJ* 2010;341:c5150

GASTRO-OESOPHAGEAL REFLUX

Physiological or pathological?

The evidence for using off label drugs in children with gastro-oesophageal reflux is poor.¹ However, the first step is to differentiate physiological gastro-oesophageal reflux from pathological gastro-oesophageal reflux disease. Many symptoms commonly attributed to the pathological disease (crying, regurgitation, feeding refusal, wheezing) may more appropriately be attributed to a mismatch between parents and paediatricians concerning the biological events.²

A misdiagnosis of gastro-oesophageal reflux disease results in unjustified and ineffective prescription of anti-reflux treatment and elimination diets, which may confuse the family and lead to the baby refusing food or developing other effects such as lower respiratory tract infections.³ The largely inappropriate prescription of proton pump inhibitors in children with physiological gastro-oesophageal

reflux has been reported and is confirmed by the more than sevenfold increase in prescriptions in infants from 1999 to 2004.⁴

When gastro-oesophageal reflux disease is diagnosed and proved—for example, in children with cerebral palsy or oesophageal atresia—only omeprazole has a paediatric indication in Europe, all other proton pump inhibitors being off label. The appropriateness of treatment with proton pump inhibitors is based on a large body of clinical evidence,⁵ and in the United States esomeprazole, lansoprazole, and omeprazole are currently authorised for children apart from infants and neonates. Regulatory agencies should translate clinical evidence into clinical practice and provide a formal paediatric indication, with ethical committees avoiding unnecessary trial replication.

Federico Marchetti clinical paediatrician
marchetti@burlo.trieste.it
Gianluca Tornese

Alessandro Ventura, Department of Paediatrics, Institute of Child Health, IRCCS Burlo Garofolo, University of Trieste, Via dell'Istria 65/1, 34100 Trieste, Italy

Competing interests: None declared.

- 1 *Drug and Therapeutics Bulletin*. Managing gastro-oesophageal reflux in infant. *BMJ* 2010;341:c4420. (27 August.)
- 2 Tornese G, Maschio M, Marchetti F, Ventura A. To GERD or not to GERD, this is the question. *J Pediatr* 2009;155:601.
- 3 Ventura A, Marchetti F, Cannioto Z, Barbi E, Martellosi S. Feeding difficulties in infants: how much a iatrogenic condition? [eLetter] *Arch Dis Child* 2008. Available at: http://adc.bmj.com/content/93/2/164/reply#archdischild_el_6549.
- 4 Barron JJ, Hiangkiat T, Spalding J, Bakst AW, Singer J. Proton pump inhibitor utilization patterns in infants. *J Pediatr Gastroenterol Nutr* 2007;45:421.
- 5 Tafuri G, Trotta F, Leufkens HGM, Martini N, Saggiocca L, Traversa G. Off-label use of medicines in children: can available evidence avoid useless paediatric trials? The case of proton pump inhibitors for the treatment of gastroesophageal reflux disease. *Eur J Clin Pharmacol* 2009;65:209-16.

Cite this as: *BMJ* 2010;341:c5155

Issues in clinical practice

The clinical review on managing gastro-oesophageal reflux in infants reports that postural treatment (elevating the head end of the crib) is ineffective.¹ However, there is evidence that management of clinically significant gastro-oesophageal reflux disease should start with a non-pharmacological approach.² This entails reducing feed volume with frequent feeding and controlled postural treatment in which the infant is nursed at 40 degrees supine to reduce regurgitation, acid reflux, and reflux associated symptoms.

Most infants referred with suspected gastro-oesophageal reflux disease to the feeding clinic at this hospital are treated with alginate combinations. Prescribing clinicians should, however, be aware of the sodium content of compound alginate combinations. Gaviscon Infant, for example, contains 0.92 mmol sodium

in each dose, so an infant having 5-6 feeds a day would receive an additional sodium load of 4.5-5.5 mmol daily, which may account for some of the constipation observed in treated infants.

Nisar A Mir consultant paediatrician, Warrington and Halton Hospitals NHS Foundation Trust, Warrington Hospital, Warrington, Cheshire WA5 1QG nisar.mir@whh.nhs.uk

Competing interests: None declared.

- 1 *Drug and Therapeutics Bulletin*. Managing gastro-oesophageal reflux in infant. *BMJ* 2010;341:c4420. (27 August.)
- 2 Vandenplas Y, De Schepper J, Verheyden S, Devreker T, Franckx J, Peelman M, et al. A preliminary report on the efficacy of the Multicare AR-Bed in 3-week-3-month-old infants on regurgitation, associated symptoms and acid reflux. *Arch Dis Child* 2010;95:26-30.

Cite this as: *BMJ* 2010;341:c5158

TREATING PREHYPERTENSION

Citizens' juries in health care

Moynihan raises a crucial question: how can we set up independent and broadly representative panels that can deliberate matters away from the long shadow of the drug industry?¹ After years of promoting citizens' and patients' participation in healthcare decisions,² we propose including citizens in deciding healthcare issues of public interest. We agree with the call for a stronger role of society, particularly when people are at risk of being labelled "sick."³ This call is consistent with an Italian project of deliberative democracy called *Giurie dei cittadini*, planned within the PartecipaSalute project.²

This project will organise citizens' juries to deliberate whether offering prostate cancer screening to all men aged 50 and older is worth while. Citizens will be given complete, plain, evidence based information and critical appraisal instruments, as well as being offered consultations with experts with differing views. Everyone involved will be required to declare conflicts of interest. The aim is to define a reproducible method for critical issues such as criteria for including citizens, criteria for selecting the information and the experts, and the outcome of the deliberation.

The project has been conceived with a healthcare public agency, local public health offices, a not for profit and a private foundation, and a medical society. It is currently under funding review.



DAVID YOUNG-WOLFF/GETTY

Lay people should be involved in public healthcare decisions, especially when uncertainty about risks and benefits is high and different values need to be elicited democratically.

Cinzia Colombo researcher, Laboratory for Medical Research and Consumer Involvement, Mario Negri Institute, via La Masa 19, 20156 Milan, Italy
cinzia.colombo@marionegri.it

Roberto Satolli editor in chief, *Zadig*, via Calzecchi 10, 20133 Milan

Alessandro Liberati associate professor and director, University of Modena and Reggio Emilia, Italian Cochrane Centre, Mario Negri Institute, via La Masa 19, 20156 Milan, Italy

Paola Mosconi head, Laboratory for Medical Research and Consumer Involvement, Mario Negri Institute, via La Masa 19, 20156 Milan, Italy

On behalf of the *Giurie dei cittadini* Working Group

Competing interests: None declared.

- 1 Moynihan R. Who benefits from treating prehypertension? *BMJ* 2010;341:c4442. (24 August.)
- 2 Mosconi P, Colombo C, Satolli R, Liberati A. PartecipaSalute, an Italian project to involve lay people, patients' associations and scientific-medical representatives on the health debate. *Health Expect* 2007;10:194-204.
- 3 Godlee F. Are we at risk of being at risk? *BMJ* 2010;341:c4766. (2 September.)

Cite this as: *BMJ* 2010;341:c5141

Be careful what you wish for

Extending the judgment of what should be considered worthy of intervention outside the medical profession and interested parties could prove interesting. Moynihan begs the question of what wider body should be given this responsibility.¹

What most people want when they are well is to be left alone to pursue their interests without interference, however well meaning. When they fall ill they want a swift, effective, and preferably painless and permanent cure. This explains the public generosity to charities collecting in the name of cancer research and cures. It is interesting to see the proliferation of charitable helicopter air ambulance schemes, which must surely be one of the least cost effective interventions imaginable.

Expanding the social group responsible for defining the area of legitimate interest for medical intervention to the wider public may result in an alteration in practice that Moynihan and other right thinking folk might find most objectionable. Just look at what national politicians do when the National Institute for Health and Clinical Excellence (NICE) decides against an expensive and only modestly effective drug. Now imagine how that would wash with parish and county councillors included in the mix of decision makers.

Christopher M Rayner retired general practitioner, Bramley, Surrey c.rayner@ukonline.co.uk

Competing interests: CMR has a small number of shares in Glaxo Wellcome to which he pays no attention whatever.

- 1 Moynihan R. Who benefits from treating prehypertension? *BMJ* 2010;341:c4442. (24 August.)

Cite this as: *BMJ* 2010;341:c5142