LETTERS

Letters are selected from rapid responses posted on bmj.com. After editing, all letters are published online (www.bmj.com/archive/sevendays) and about half are published in print
To submit a rapid response go to any article on bmj.com and click "respond to this article"

BODYBUILDING SUPPLEMENTS

Is tamoxifen being sold to bodybuilders?

For more than 30 years, bodybuilders have taken tamoxifen to prevent and treat gynaecomastia caused by use of anabolic steroids.[1 2] Usually, tamoxifen is sourced from the illicit market. However, bodybuilding discussion forums have speculated that a dietary supplement called Esto Suppress contains tamoxifen because the label listed one of its chemical names (figure). Four samples were purchased at different times between late 2011 and early 2012 and were analysed using reference standards and gas chromatography coupled with flame ionisation and mass spectrometry detectors. Tamoxifen was found in samples 1 (3.8 mg), 2 (0.9 mg), and 3 (3.0 mg), but not in sample 4. The product label suggested a dosage of two capsules a day, which in the case of sample 1 may have provided 7.6 mg of tamoxifen; 10-20 mg is used clinically for treating gynaecomastia.[3] It is not known whether the Esto Suppress currently being sold still contains tamoxifen.

Since the 2000s, a growing number of off-the-shelf "food," "herbal," or "dietary" "supplements"—aimed at gym goers and people wanting to lose weight or enhance their sex lives—have contained pharmacologically active substances.[2] These include anabolic steroids, erectogenics, stimulants, appetite suppressants, and anxiolytics.[2 4] Some of these substances have been withdrawn from use in medicines owing to safety concerns, others have never been tested in humans. Often the substances are not listed on the labelling, and products may be marketed as "natural," exploiting the belief that they are safer and healthier options.[5] In other cases, such as with Esto Suppress, only an obscure reference is made to the substance, such as a chemical name. Most users will be unaware that they are taking these substances. Healthcare professionals should ask their patients about their use of "supplements" and report suspected adverse reactions (in the UK: https://yellowcard.mhra.gov.uk).

Esto Suppress containing tamoxifen

Michael Evans-Brown scientific analyst, European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), Lisbon, Portugal
Michael.Evans-Brown@emcdda.europa.eu
Andreas Kimergård visiting lecturer
Jim McVeigh deputy director
Martin Chandler human enhancement drugs researcher
Simon D Brandt reader in bioactive drug chemistry, School of Pharmacy and Biomolecular Sciences, Liverpool John Moores University, Liverpool, UK
Competing interests: None declared.
Full response at: www.bmj.com/content/344/bmj.e468/rr/683699..
1 Spano F, Ryan WG. Tamoxifen for gynecomastia induced by anabolic steroids? *N Engl J Med* 1984;311:861-2.
2 Evans-Brown M, McVeigh J, Perkins C, Bellis MA. Human enhancement drugs. The emerging challenges to public health. North West Public Health Observatory, 2012.
3 Kunath F, Keck B, Antes G, Wullich B, Meerpohl JJ. Tamoxifen for the management of breast events induced by non-steroidal antiandrogens in patients with prostate cancer: a systematic review. *BMC Med* 2012;10:96.
4 Food and Drug Administration. Tainted_Supplements_CDER. www.accessdata.fda.gov/scripts/sda/sdNavigation.cfm?filter=&sortColumn=1d&sd=tainted_supplements_cder&page=1.
5 Ipsos MORI. Public perceptions of herbal medicine. 2008.
Cite this as: *BMJ* 2014;348:g1476

OSELTAMIVIR AND ZANAMIVIR FOR FLU

DoH's misguided alert on flu

On 27 January 2014, the Department of Health's chief medical and pharmaceutical officers, Sally Davies and Keith Ridge, wrote a "for action" alert to NHS England leads, GPs, and community pharmacies endorsing the use of the antiviral drugs oseltamivir and zanamivir for prophylaxis and treatment of flu.[1] The alert authorises GPs to prescribe the drugs at NHS expense for defined at risk groups and certain other people.

Together with now outdated National Institute for Health and Care Excellence guidance,[2] the alert ignores the authoritative Cochrane review that shows the inadequacy of the underpinning evidence.[3] It also ignores multiple side effects of these drugs listed on prescribing information, as well as the recent National Audit Office report on the uncertain benefits of these drugs and the huge amounts of health funds spent then wasted when stockpiled supplies were destroyed.[4]

The AllTrials initiative for open access to drug trial data has exposed the scandal of incomplete presentation and concealment of data on oseltamivir and zanamivir, the drugs endorsed by this alert. The Cochrane review showed that data from 60% of people involved in phase III trials of oseltamivir were never published. This included the biggest treatment trial ever undertaken on oseltamivir that included just over 1400 people of all ages; these data remain unavailable for scrutiny by the scientific community.[3]

This alert inflicts risk on the public. It supports drug manufacturers, not the evidence based care of patients and cost effective use of NHS funds.

We urge the Department of Health to withdraw the alert; insist that the drug industry puts all the evidence in the public domain; and review and publish the evidence so that prescribers, pharmacists, and the public are correctly informed about these drugs.

Patricia McGettigan clinical pharmacologist, William Harvey Research Institute, Barts and the London School of Medicine and Dentistry, London EC1M 6BQ, UK p.mcgettigan@qmul.ac.uk
Allyson Pollock professor, Global Health, Policy and Innovation Unit, Queen Mary, University of London, UK
Andrew Herxheimer emeritus fellow, Cochrane Collaboration, London, UK
Competing interests: None declared.
Full response at: www.bmj.com/content/348/bmj.g13/rr/686055.
1 Davies SC. Influenza season 2013/14—use of antiviral medicines.
2 National Institute for Health and Care Excellence. Influenza—zanamivir, amantadine and oseltamivir.
3 Jefferson T, Jones MA, Doshi P, Del Mar CB, Heneghan CJ, Hama R, et al. Neuraminidase inhibitors for preventing and treating influenza in healthy adults and children. *Cochrane Database Syst Rev* 2012;1:CD008965.
4 National Audit Office. Access to clinical trial information and the stockpiling of Tamiflu. 2013.
Cite this as: *BMJ* 2014;348:g1594

AUTOIMMUNE ENCEPHALITIS

Autoimmune encephalitis on non-psychiatric wards in the UK

Autoimmune encephalitis is increasingly recognised as a cause of acute psychiatric disturbance. Affected patients usually require admission to a neurology ward for assessment and treatment, and they often display serious psychiatric symptoms and disturbed behaviour.[1-3]

We are worried about the safe management of these patients on non-psychiatric wards. Although "organic," these conditions manifest in a similar way to functional psychoses. They require the expertise of psychiatrists and allied professionals and a safe physical milieu for appropriate management and use of the Mental

Health Act where indicated. In our experience, the behavioural management of these patients on neurology wards is often difficult, and physical harm has occurred to patients themselves, fellow patients, and staff.

It would not be feasible to place these patients in psychiatry units because of the need for neurological assessment and physical treatments. However, in the UK, psychiatric inpatient units are often distant from acute hospitals and the operational systems surrounding psychiatry and neurology differ. Staff on neurological wards are less skilled in the management of disturbed patients. It is often impossible to find registered mental health nurses. Security guards have occasionally been used, but we believe that this is far from ideal. Provision of liaison psychiatry services is inconsistent and neuropsychiatric inpatient facilities are limited.

This problem deserves prompt attention, particularly as an increasing proportion of psychiatric illnesses will probably be found to be neurological. Possible steps towards resolving the current situation include providing acute medical/neurological beds within areas designed to minimise physical risk, increasing psychiatric training for neurologists and neurological nurses, and increasing the availability of neuropsychiatric expertise and specialist neuropsychiatry units with staff trained in both mental and physical healthcare.

Nicholas Moran consultant neurologist, Department of Neurology, Kent and Canterbury Hospital, Canterbury CT1 3NG, UK
Neil Munro consultant neurologist, Department of Neurology, William Harvey Hospital, Ashford, UK
Kirsten Lawson clinical lead liaison psychiatry, Kent and Medway NHS and Social Care Partnership Trust, Maidstone, UK
Anthony S David professor of cognitive neuropsychiatry, Institute of Psychiatry, King's College London, London, UK
Competing interests: None declared.
Full response at: www.bmj.com/content/344/bmj.e468/rr/685376.

1 Dalmau J, Gleichman AJ, Hughes EG, Rossi JE, Peng X, et al. Anti-NMDA-receptor encephalitis: case series and analysis of the effects of antibodies. *Lancet Neurol* 2008;7:1091-8.
2 Vincent A, Buckley C, Schott JM, Baker I, Dewar BK, Detert N, et al. Potassium channel antibody-associated encephalopathy: a potentially immunotherapy-responsive form of limbic encephalitis. *Brain* 2004;127:701-12.
3 Pollak TA, McCormack R, Peakman M, Nicholson TR, David AS. Prevalence of anti-N-methyl-d-aspartate (NMDA) antibodies in patients with schizophrenia and related psychoses: a systematic review and meta-analysis. *Psychol Med* (forthcoming).

Cite this as: *BMJ* 2014;348:g1466

INTRAVENOUS FLUID REPLACEMENT

Dangers of overhydration in children

As opposed to my colleagues who work in developing countries,[1] I encounter the problem of overhydration on almost a daily basis.

Overzealous intravenous fluid replacement therapy is a regular feature, despite recently emerging evidence (ironically coming from developing countries) of potential harm.

The recent FEAST study found that giving children fluids slowly to maintain normal levels, rather than rapid fluid resuscitation, aids recovery more safely and effectively.[2] There is also ample published evidence of harm.[3]

These studies have problems related to external validity, but their results suggest that cautious intravenous fluid replacement is preferable to the traditional administration of fluid boluses.

As much as we need to educate patients and families about sanitation and oral rehydration, we need to educate ourselves about a potentially harmful treatment: intravenous fluid replacement therapy.

P Janos Baombe emergency medicine consultant, Royal Manchester Children's Hospital, Manchester M13 9WL, UK baombejp@yahoo.co.uk
Competing interests: None declared.

1 Parashar UD, Nelson EAS, Kang G. Diagnosis, management, and prevention of rotavirus gastroenteritis in children. *BMJ* 2013;347:f7204. (30 December.)
2 Fluid Expansion As Supportive Therapy (FEAST). Publications and references. www.feast-trial.org/publications.
3 Maitland K, Kiguli S, Opoka RO, Engoru C, Olupot-Olupot P, Akec SO, et al. Mortality after fluid bolus in African children with severe infection. *N Engl J Med* 2011;364:2483-95.

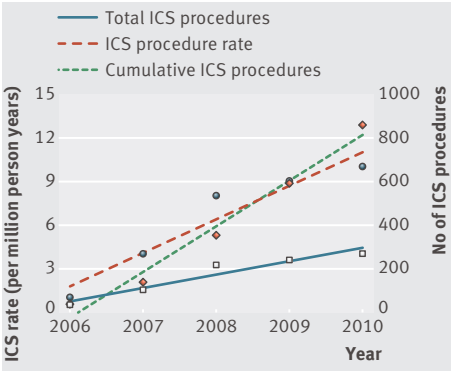
Cite this as: *BMJ* 2014;348:g1569

WINGSPAN SAGA

Adoption of Wingspan stents

Two recent *BMJ* articles have criticised the US Food and Drug Administration for approving the Wingspan stent used for intracranial stenting (ICS) to prevent recurrent stroke despite insufficient evidence of its effectiveness.[1 2] They also draw attention to the FDA's inadequate response to recent evidence from the SAMMPRIS randomised controlled trial against the use of ICS in these patients.

We share these concerns and would like to draw attention to additional evidence that we published in 2013 on the adoption and outcomes of this technology in a 100% Medicare population during 2006 to 2010.[3] We found limited adoption of the technology during that time—826 Medicare fee-for-service beneficiaries received ICS, increasing from 1 per 1 000 000 person years (35 procedures) in 2006 to 9 per 1 000 000 person years (258 procedures) in 2010 (figure). The increase, however, was modest and we attributed this limited adoption to a highly restrictive reimbursement policy by the Centers for Medicare and Medicaid Services (CMS), which provided coverage for this procedure only in the context of a randomised trial. We compared this with endovascular devices for mechanical embolectomy in patients with acute stroke



Numbers of intracranial stenting (ICS) procedures and rate per million person years, 2006-10

that were approved through the FDA's 510(k) pathway and are fully reimbursed by CMS, which led to a much more rapid rate of increase in their use in recent years.

We also showed that 30 day mortality increased from 2.9% in 2006 to 12.9% in 2010 (P=0.1). Our database did not allow comparison with patients who received medical management alone, restricting any conclusion about the safety or efficacy of this procedure. Unfortunately, nine years after approval, despite inconclusive evidence, this device continues to be available, with only a safety communication issued by FDA in 2012.

Aakriti Gupta internal medicine resident, Yale-New Haven Hospital, New Haven, CT 06511, USA aakriti.gupta@yale.edu
Harlan Krumholz professor of medicine (cardiology), Yale New Haven Hospital Center for Outcomes Research and Evaluation, New Haven, CT, USA
Competing interests: None declared.
Full response at: www.bmj.com/content/348/bmj.g93/rr/684818.

1 Gartenberg AJ, Peleg A, Dhruva SS, Redberg RF. Presumed safe no more: lessons from the Wingspan saga on regulation of devices. *BMJ* 2014;348:g93. (22 January.)
2 Cohen D. Cardiologists criticize US regulator for keeping intracranial stent on market. *BMJ* 2014;348:g357. (22 January.)
3 Gupta A, Desai MM, Kim N, Bulsara KR, Wang Y, Krumholz HM. Trends in intracranial stenting among Medicare beneficiaries in the United States, 2006-2010. *J Am Heart Assoc* 2013;2:e000084.

Cite this as: *BMJ* 2014;348:g1552

ARE WE OVERUSING IVF?

More older women present as unexplained subfertility

Kamphuis and colleagues report that the incidence of unexplained subfertility as an indication for IVF has undoubtedly increased,[1] but why? The most likely reason is the increase in female childbearing age and ovarian senescence in older women presenting as unexplained subfertility.[2]

The proportion of older women seeking IVF and the proportion of IVF cycles offered for unexplained subfertility have increased in parallel.[1 3] Human

biology dictates that the chances of conception decrease with advancing female age. Although the success of IVF has increased greatly over the years with advances in technology, success in women aged 40 years or more has changed little, with live birth rates being less than 10%.[3] However, many couples view IVF as a "fix all" for voluntarily postponing childbearing.

Is IVF a cure for ovarian senescence, which is often diagnosed as unexplained infertility in older women? What is the management pathway for fertility in these women? The studies cited by Kamphuis and colleagues on natural conception rates in women with unexplained subfertility involve younger women,[4 5] and it would be incorrect to extrapolate their findings to older women. Paucity of evidence to guide management of the ever increasing numbers of older women seeking fertility treatment is perhaps leading to IVF being overused.

Could the epidemic of ovarian ageing and subfertility be tackled by promoting fertility awareness among women and society? Education would help with health economics and might be a remedy for "too much medicine."

Sesh Kamal Sunkara subspecialist in reproductive medicine, Queen Elizabeth Hospital, King's Healthcare Partners (Guy's and St Thomas NHS Foundation Trust), London, UK
sksunkara@hotmail.com
Srividya Seshadri subspecialist in reproductive medicine, Guy's Hospital, London, UK
Competing interests: None declared.
Full response at: www.bmj.com/content/348/bmj.g252/rr/685548.

1 Kamphuis EI, Bhattacharya S, van der Veen F, Mol BWJ, Templeton A; for the Evidence Based IVF Group. Are we overusing IVF? *BMJ* 2014;348:g252. (28 January.)
2 Maheshwari A, Hamilton M, Bhattacharya A. Effect of female age on the diagnostic categories of infertility. *Hum Reprod* 2008;23:538-42.
3 Fertility treatment in 2011. Trends and figures. Human Fertilisation and Embryology Authority.
4 Brandes M, Hamilton CJ, van der Steen JO, de Bruin JP, Bots RS, Nelen WL, et al. Unexplained infertility: overall ongoing pregnancy rate and mode of conception. *Hum Reprod* 2011;26:360-8.
5 Steures P, van der Steeg JW, Hompes PG, Habbema JD, Eijkemans MJ, Broekmans FJ, et al. Intrauterine insemination with controlled ovarian hyperstimulation versus expectant management for couples with unexplained subfertility and an intermediate prognosis: a randomised clinical trial. *Lancet* 2006;368:216-21.

Cite this as: *BMJ* 2014;348:g1583

WHERE THERE'S SMOKE . . .

Air pollution in Iran

Brauer and Mancini say that "nowhere are the health effects of outdoor air pollution felt more than in China."[1]

But four of the top 10 air polluted cities are in Iran. Ahvaz is the most polluted city in the world, with particulate levels three times that of Beijing, and nearly 13 times that of London.[2] Ahvaz struggles with micro-dust blowing in from neighbouring countries, as well as industrial and domestic pollution.

Tehran has cleaned up recently, with carbon monoxide levels no longer a problem, lead eliminated from gasoline, and sulphur levels dropping from a frightening 8000 parts per million (ppm) to less than 200 ppm (they are aiming at <10). But a third of days in Tehran are still officially "unhealthy." It's worse for the vulnerable—schools are often closed.

Sanctions make it difficult for Iranians to improve things: petroleum sanctions mean they are forced to use their own "wrong sort of petrol" for everything. Financial sanctions mean that there is no money for "best available technology," even if imports were allowed. So they can't retrofit urban buses or think about hybrid electric taxis and motorbikes, as they would like to. They can't even import the calibration gases needed for their monitoring programme.[3] At a recent Iran Heritage Foundation conference, there was talk of donkeys smuggling these high technology gases over the mountain borders.[4]

Micro-dust is also "exported" from Iran. The complete drying out of Iran's third largest lake (once 388 500 km^2) has led to major population movements, with many adverse health effects. The consequent dust blows hundreds of kilometres into the eyes and lungs of those in Pakistan and Afghanistan.[5]

Caroline Mawer urgent care GP, London, UK
caroline.mawer@gmail.com
Competing interests: None declared.
Full response at: www.bmj.com/content/348/bmj.g40/rr/685423.

1 Brauer M, Mancini GBJ. Where there's smoke . . . *BMJ* 2014;348:g40. (21 January.)
2 WHO. Database: outdoor air pollution in cities: 2003-10.Hosseini V. Air pollution: causes, effects and mitigating measures. Presented at Iran's Natural Heritage: A Catalyst Symposium to Spark Measurable Change, 18-19 January 2014. www.youtube.com/embed/nJKgufsEgl8.
3 Iran Heritage. Conference summary. 2014.
4 Lewis G. Saving the imperiled Hamouns of Eastern Iran. UNDP, 2014.

Cite this as: *BMJ* 2014;348:g1586

HUMAN RIGHTS AND THE GMC

Doctors should be protected by the Human Rights Act too

Public perception of the medical profession is important. Occasionally this is jeopardised through misconduct that leads to possible cautions or convictions. The General Medical Council typically discovers misconduct through self declaration, patient concern, and Disclosure and Barring Service (DBS) checks.[1]

In early 2013, the European Court declared that the UK wasn't operating within the confines of the Human Rights Act Section 8.[2] As such, a filtering process was implemented on 29 May 2013, meaning certain cautions and convictions, after a set time period, couldn't be disclosed on DBS checks to employers.[3] Furthermore, legislation change made it illegal for employers to ask questions that might lead employees to disclose filtered offences.[3]

This remains unpublicised by the GMC. *Good Medical Practice* came into effect on the 22 April 2013,[4] shortly before the change in law, but it does not reflect the changes, despite them being well cited in the media. It is unclear whether professional bodies can ask for filtered offences to be declared, but most interested organisations argue that this is not the case,[6] and even if it were, it is still illegal for the check to disclose filtered offences.[5]

Additionally, the Foundation Programme Application System failed to acknowledge the new legislation by asking the 2013-14 cohort of final year students to answer a criminal records declaration question on a form produced in 2011,[3] leading all applicants to consider a question that breaches their human rights.

Both organisations are ignoring recent legislation to protect doctors' and medical students' human rights. Obviously, reproducing forms is costly, but when so little effort has been made to make people aware of these changes, I wonder who is looking after our rights.

Thomas Lemon medical student, School of Medicine, Cardiff University, Cochrane Building, University Hospital of Wales, Cardiff CF14 4XW, UK
lemonti@cf.ac.uk
Competing interests: I am a Foundation Programme Application System (FPAS) applicant.
Full response at: www.bmj.com/content/347/bmj.f6836/rr/680160.

1 BMA. Criminal records checks. http://bma.org.uk/practical-support-at-work/contracts/criminal-records-checks.
2 Peachey P. Court of appeal rules CRB check law must go. *Independent* 2014. www.independent.co.uk/news/uk/home-news/a-breach-of-human-rights-court-of-appeal-rules-crb-check-law-must-go-8471325.html.
3 Her Majesty's Government. Filtering guide. www.gov.uk/government/uploads/system/uploads/attachment_data/file/266123/Filtering_guide_v2.3.pdf.
4 General Medical Council. Good medical practice. 2013. www.gmc-uk.org/static/documents/content/GMP_2013.pdf_51447599.pdf.
5 Nacro. Filtering legislation. www.nacro.org.uk/what-we-do/resettlement-advice-service/advice/disclosure-legislation/filtering-legislation,1648,NAP.html.

Cite this as: *BMJ* 2014;348:g1549

GMC's reply

Lemon makes an important point about doctors' and medical graduates' obligations to declare previous convictions. He is right to suggest that the General Medical Council must comply with the law and respect human rights. We are aware of recent changes that prohibit organisations like us from using information about certain convictions, and we have complied with the new provisions in every case since the changes took effect. We are also aware of the need to amend our guidance for registration applicants to make absolutely clear what information we do and do not require, and we are currently

working with the National Association for the Care and Resettlement of Offenders on this.

The GMC's primary concern is patient protection, and it is right that our registration processes are stringent. We will continue with that approach while respecting doctors' and medical graduates' human rights.

Niall Dickson chief executive, General Medical Council, London NW1 3JN, UK lhadjiconstanti@gmc-uk.org
Competing interests: None declared.
Cite this as: *BMJ* 2014;348:g1550

BAD MEDICINE: THE RISE OF DULOXETINE

Author's reply

Pain is indeed an important issue. But the current definition—"pain is what the patient says it is"—is far too loose (next letter, the Response).[1] The reported incidence of pain varies 10-fold by country,[2] so this definition is simply biologically implausible. Pain is cultural, not merely medical, and it is the major medically unexplained symptom. To suggest that one in five adults has chronic pain is counterintuitive, defying common sense and experience. If we do not challenge this definition, flawed epidemiology, and flawed research, we risk widespread medicalisation.

The US and other parts of the world are in the grip of an epidemic of deaths linked to these flawed assumptions and overuse of opioid drugs for pain.[2] There are also increasing concerns about the dangers of gabapentoids.[3] Today dangerous polypharmacy is the norm, not the exception, in pain management, but some in the international pain community seem unwilling to accept these concerns. Emotional defensiveness helps no one.

As for "declared interests," these are the same as "conflicts of interest." Such links to Big Pharma are the rotten core of modern medicine and give us a blinkered therapeutic mindset. And a positive Cochrane review is an endorsement—a medical marketing department gift. For pain is big business, offering companies polypharmacy of lifelong branded drugs.

Duloxetine may be effective for some who have a narrow and definable condition such as diabetic neuropathy. The point of my article was to express concern over the rapid rise of duloxetine prescribing and its potential use in unlicensed pain syndromes.[1] I passionately believe that we have a duty to those who are sick but an equal duty to protect those who are well from iatrogenic harm.

Des Spence general practitioner, Glasgow G20 9DR, UK destwo@yahoo.co.uk
Competing interests: None declared.

1 Spence D. Bad medicine: the rise of duloxetine. *BMJ* 2014;348:g139. (17 January.)
2 Spence D. Bad medicine: the painful truth: deaths and misuse of prescribed drugs. *BMJ* 2011;343:d7403.
3 Spence D. Bad medicine: gabapentin and pregabalin. *BMJ* 2013;347:f6747.(8 November.)

Cite this as: *BMJ* 2014;348:g1515

RESPONSE

Duloxetine: Andrew Moore and colleagues reply to Des Spence

Spence's polemic on duloxetine loses power because most of what it is based on is wrong.[1] Making pronouncements in respected journals about good and bad medicine comes with the responsibility of knowing what you are talking about. Bad scholarship helps no one, especially those in pain; research in genetics, neurobiology, and psychology has contributed to huge advances in knowledge about the bio-psycho-social origins of pain.

Chronic pain is defined as pain of moderate or severe intensity that lasts for three months or more (think of a really bad headache lasting from Christmas to Easter). It affects one in five adults. Painful conditions are among the most prevalent conditions and are five of the top 11 in terms of years living with disability. Chronic pain destroys lives, has a huge negative impact on quality of life, is costly, reduces the ability to work or function inside the family, and may be associated with decreased life expectancy.

Here is a brief, non-comprehensive list of where Spence misses the point.

Women are not over-represented in trials. Chronic pain disproportionately affects women; their representation matches the epidemiology.

Pain is the most immediate of patient outcome measures, reported by patients themselves. Its subjectivity was recognised in the 1950s and dealt with. Different scales show excellent agreement, and patients in clinical trials record consistent pain levels over long periods, as in clinical practice.

Average benefits over placebo are in the order of 1 point on a 10 point rating score. But few patients are average; most have either little or great benefit. A responder is defined as someone with at least a 50% reduction in pain intensity maintained for 12 weeks, without intolerable adverse events that mean stopping treatment. Patients want this outcome, and it is accompanied by major improvements in sleep, function, and quality of life.

Cochrane reviews do not report effective non-drug alternatives. One of exercise in fibromyalgia involved only 223 patients in four small trials of barely adequate quality; another of psychological therapies found that effects are at best weak and that more research is urgently needed.[2]

Cochrane reviews endorse nothing.[3] Several large good quality trials provide good evidence that duloxetine is effective in painful diabetic neuropathy and fibromyalgia. The effect size is not massive—a number needed to treat of five tells you that—but it is comparable to other treatments in neuropathic and other chronic pain, where treatment failure is expected more often than treatment success.[4]

We are not "steeped in conflicts of interest." Some (but not all) make declarations of interest, not the same as conflicts. We are proud of this, when it means bringing unpublished information into the public domain, accessing data at the level of the individual patient to improve understanding of outcomes, and, importantly, demonstrating new sources of large potential bias. Our rule over 30 years is that we work only with organisations that agree an unrestricted right to publish the results, whatever they may be.

Spence omits the most important, valid, criticisms. These might include the bias against older treatments because authorities require trials fundable only by industry or government (which neither fund). Effective drugs like amitriptyline are understudied so have less evidence of efficacy to support their use. In addition, inappropriate imputation methods in statistical analysis of results can mean that efficacy is sometimes hugely inflated[5]; this is not the case for duloxetine.[6]

Patients need options. Encouraging people to act against the evidence is the real "bad medicine."

Andrew Moore honorary senior research fellow andrew.moore@ndcn.ox.ac.uk
Phil Wiffen honorary professor, Pain Research and Nuffield Division of Anaesthetics, Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford OX3 7LE, UK
Christopher Eccleston professor, Centre for Pain Research, University of Bath, Bath, UK
Michael Lunn consultant neurologist
Richard Hughes honorary professor, National Hospital for Neurology and Neurosurgery and MRC Centre for Neuromuscular Diseases, London, UK
Amanda Williams clinical reader, Research Department of Clinical, Educational, and Health Psychology, University College London, London, UK
Dominic Aldington consultant anaesthetist, consultant in pain management, Royal Hampshire County Hospital, Winchester, UK
Eija Kalso professor, Institute of Clinical Medicine, Faculty of Medicine, University of Helsinki and Pain Clinic, Department of Anaesthesia and Intensive Care Medicine, Helsinki University Central Hospital, Helsinki, Finland
Competing interests: ML, RH, and PW wrote a Cochrane review on duloxetine. AM has received honorariums for consulting from Eli Lilly. AM, DA, and EK were authors of a *BMJ* article criticised by Spence. CE and AW declare no conflicts.
Full response, including references, at: www.bmj.com/content/348/bmj.g139/rr/685335.
Cite this as: *BMJ* 2014;348:g1490