



Tamiflu, pp 1321, 1342, 1348, 1352, 1364



March against climate change, p 1335



Our Christmas MSF campaign, p 1341



Different strokes for different folks, p 1379

## EDITORIALS

- 1321 Why don't we have all the evidence on oseltamivir?**  
The full data from drug trials must be available for scrutiny, say Fiona Godlee and Mike Clarke  
» *Letters*, p 1330, *Feature*, p 1342  
» *Analysis*, pp 1348, 1352  
» *Research*, p 1364
- 1323 Subclinical hypothyroidism after pre-eclampsia**  
High concentrations of antiangiogenic factor may impair thyroid function during and after pregnancy, say Robyn A North and Robert N Taylor  
» *Research*, p 1355
- 1324 Losing weight in moderate to severe obstructive sleep apnoea**  
Can benefit more than half of patients, say Nathaniel S Marshall and Ronald R Grunstein  
» *Research*, p 1365
- 1326 Heroin assisted treatment**  
Should be a routine last resort in patients with opioid dependence refractory to standard treatments, says Wim van den Brink

## LETTERS

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- 1328 PSA and prostate cancer; Dengue**
- 1329 Whitehall study; Quality in a poorer NHS; Whistleblowing**
- 1330 Response: Roche replies to the Cochrane review on oseltamivir**

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- 1331 Doctors had warned of understaffing at hospital where Baby P's injuries were overlooked**  
Healthcare regulators will start without chiefs
- 1332 Doctors and scientists back petition to demand reform of England's libel laws**  
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- 1333 Specialist mental health advisers are to be available in job centres to hasten recovery**  
Fear of minimum alcohol pricing spreading to other countries led to opposition in Scotland
- 1334 Working environment is to blame for drug errors**  
Fall in swine flu may not signal end of epidemic
- 1335 UK doctors unite to combat climate change**
- 1336 The mysterious Dr Foster**
- 1337 Measles deaths fall 78% worldwide, 2000-8**

## SHORT CUTS

- 1338 What's new in the other general journals**

## OBSERVATIONS

- LIFE AND DEATH**
- 1340 A tribute to George Godber** Iona Heath
- BMJ CHRISTMAS CHARITY APPEAL**
- 1341 Please help support Médecins Sans Frontières** Fiona Godlee

## FEATURES

- 1342 Complications: tracking down the data on oseltamivir**  
A Cochrane group's attempt to reproduce an analysis underpinning the use of oseltamivir in pandemic influenza hit a brick wall. Deborah Cohen retraces its steps

## ANALYSIS

- 1348 Neuraminidase inhibitors: the story behind the Cochrane review**  
Although billions have been spent on oseltamivir in the face of pandemic influenza, the team updating the Cochrane review of neuraminidase inhibitors in healthy adults found that the public evidence base for this global public health drug was fragmented and inconsistent. Peter Doshi tells the story
- 1352 What can we learn from observational studies of oseltamivir to treat influenza in healthy adults?**  
Post-marketing studies can provide important information about safety and efficacy in real practice. However, Nick Freemantle and Mel Calvert found studies of oseltamivir identified by Roche were of limited value

## RESEARCH, CLINICAL REVIEW, AND PRACTICE

 See next page

## OBITUARIES

- 1377 Angelo M DiGeorge; Arend Jan Dunning; Cyril Forssander; James Howard Lewis; James Lionel Somervell; Arthur Powell Wyatt; Michael Ernest Nicholas Anfilogoff; John Roslyn Anthony**

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### PERSONAL VIEW

- 1379 A lesson learnt** Sharon Elizabeth Whitehorn

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- 1380 Behind the pages of clinical research** Allen Shaughnessy

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- 1381 A grave matter** Theodore Dalrymple

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- 1381 The Canon of Medicine (Al-Qanun fi'l-tibb)** by Ibn Sīnā (Avicenna) Gavin Koh

### COLUMNISTS

- 1382 Goodbye to the noughties** Des Spence  
**Let's abandon hope** Ike Iheanacho

## ENDGAMES

- 1383 Quiz page for doctors in training**

## MINERVA

- 1384 iPhone app that tracks alcohol intake and other stories**

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- 1363 The late Matron Wardroper (1892)**

Minimum pricing for alcohol,  
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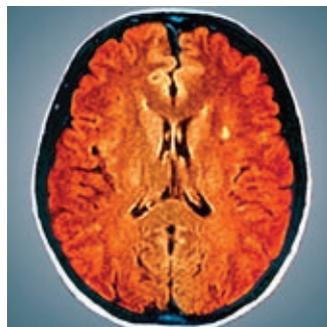




Neuraminidase inhibitors, p 1364



Severe obstructive sleep apnoea, p 1365



Multiple sclerosis, p 1359



Chest drains, p 1371

## RESEARCH

- 1355 Pre-eclampsia, soluble fms-like tyrosine kinase 1, and the risk of reduced thyroid function: nested case-control and population based study**  
Increased serum concentration of sFlt-1 during pre-eclampsia is associated with subclinical hypothyroidism during later pregnancies, and pre-eclampsia may also predispose to reduced thyroid function in later years

Richard J Levine, Lars J Vatten, Gary L Horowitz, Cong Qian, Pal R Romundstad, Kai F Yu, Anthony N Hollenberg, Alf I Hellevik, Bjorn O Asvold, S Ananth Karumanchi

» *Editorial, p 1323*

- 1359 Multiple sclerosis risk sharing scheme: two year results of clinical cohort study with historical comparator**

No firm conclusions can be drawn from this two year interim analysis on whether the UK's national 10 year scheme for prescribing expensive disease modifying treatments is cost effective for the NHS

Mike Boggild, Jackie Palace, Pelham Barton, Yoav Ben-Shlomo, Thomas Bregenzer, Charles Dobson, Richard Gray

- 1364 *pico* Neuraminidase inhibitors for preventing and treating influenza in healthy adults: systematic review and meta-analysis**

Neuraminidase inhibitors reduce the transmission of seasonal influenza and reduce the duration of symptoms by about half to one day, but published data are insufficient to know if they reduce complications or are safe

Tom Jefferson, Mark Jones, Peter Doshi, Chris Del Mar

» *Editorial, p 1321, Feature, p 1342, Analysis, p 1348*

- 1365 *pico* Effect of a very low energy diet on moderate and severe obstructive sleep apnoea in obese men: a randomised controlled trial**

Men randomised to seven weeks' treatment with a low energy liquid diet had significant reductions in obstructive sleep apnoea when compared with a control group who stuck to their usual diet

Kari Johansson, Martin Neovius, Ylva Trolle Lagerros, Richard Harlid, Stephan Rössner, Fredrik Granath, Erik Hemmingsson

» *Editorial, p 1324*

## CLINICAL REVIEW

- 1366 Hepatocellular carcinoma for the non-specialist**  
T Kumagi, Y Hiasa, G M Hirschfield

## PRACTICE

- 1371 SAFETY ALERTS**

**Insertion of chest drains: summary of a safety report from the National Patient Safety Agency**

Tara Lamont, Michael Surkitt-Parr, John Scarpello, Marcus Durand, Clare Hooper, Nick Maskell

- 1372 INTERACTIVE CASE REPORT**

**A woman with acute myelopathy in pregnancy: case outcome**

Reinhard Reuß, Paulus S Rommer, Wolfgang Brück, Friedemann Paul, Michael Bolz, Sven Jarius, Tobias Boettcher, Annette Großmann, Alexander Bock, Frauke Zipp, Reiner Benecke, Uwe K Zettl

- 1373 COMMENTARY**

**Learning out of your depth**

Ed Peile

- 1374 COMMENTARY**

**Complex medical conditions in pregnancy need appropriate multidisciplinary input**

Lucy C Chappell

- 1375 COMMENTARY**

**Managing clinicians' assessment**

Reinhard Reuß, Michael Bolz, Uwe K Zettl

- 1375 COMMENTARY**

**Patient's view**

Andrea G, with the support of Reinhard Reuß

- 1376 COMMENTARY**

**Neurological perspective**

Adam B Cohen, Matt T Bianchi

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BMA House, Tavistock Square,  
London WC1H 9JR

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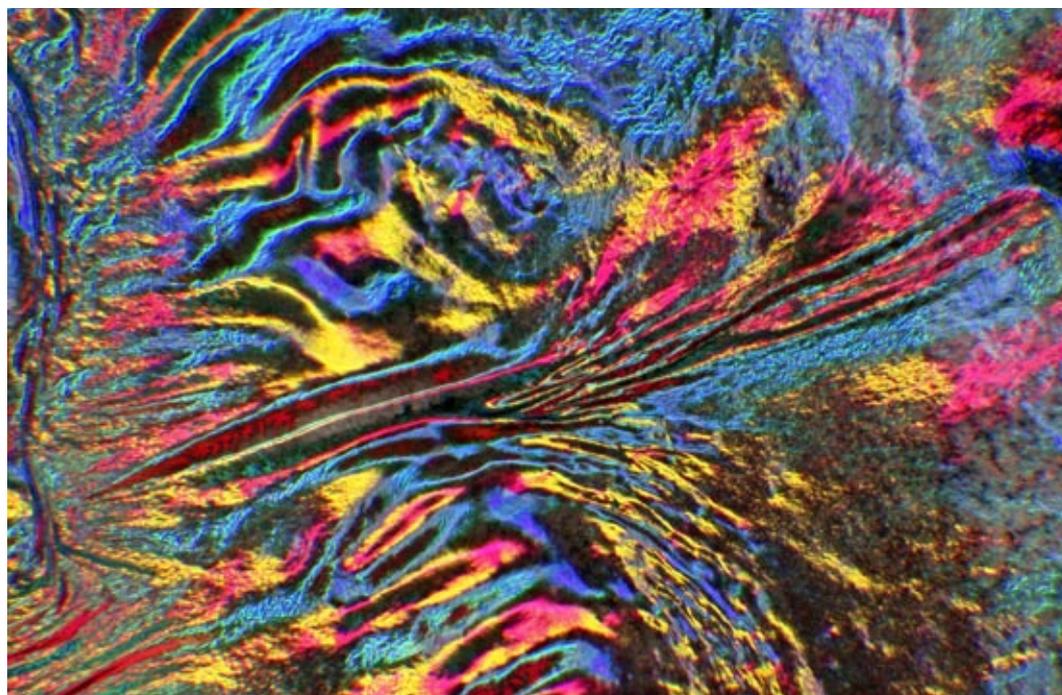
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## PICTURE OF THE WEEK

Image of crystallised contents of an oseltamivir capsule, created for the *BMJ* by the photomicrographer Spike Walker. Crossed polarising filters in light microscopy of the molten powder yield these intriguing shapes and vivid colours. Spike has won 19 Wellcome Image Awards, including five this year ([www.wellcomeimageawards.org](http://www.wellcomeimageawards.org)). For more on oseltamivir see Editorial, p 1321, Feature, p 1342, Analysis, pp 1348 and 1352, and Research, p 1364.

## THE WEEK IN NUMBERS

**50 000** People who marched to press the government to take action on climate change (News, p 1335)

**67%** Reduction in apnoea hypopnoea index in obese men allocated to very low energy diet (Research, p 1365)

**3.9** Age standardised incidence of hepatocellular carcinoma per 100 000 people in the UK (Clinical Review, p 1366)

**2 in 3** Proportion of UK trusts that had major complications associated with chest drain insertion over five years (Practice, p 1371)

**£500m** UK government spending on H1N1 drugs by October, with a commitment to spend over £1bn (Feature, p 1342)

## THE WEEK IN QUOTES

**“Women with a history of pre-eclampsia may be at increased risk of future hypothyroid function”** (Research, p 1355)

**“We are no longer sure that oseltamivir offers advantage over cheap, over the counter drugs such as aspirin”** (Analysis, p 1348)

**“George [Godber] understood that there is such a thing as society and that individuals exist within a network of mutual responsibility”** (Observations, p 1340)

**“You are well and truly fucked”** (Personal View, p 1379)

**“It is not appropriate for the alcohol industry to influence the direction of public health policy to favour private economic interests”** (News, p 1333)

## EDITOR'S CHOICE

## We want raw data, now



**Editorials, p 1321**  
**Letters, p 1330**  
**Feature, p 1342**  
**Analysis, pp 1348, 1352**  
**Research, p 1364**

This week's *BMJ* is dominated by a cluster of articles on oseltamivir (Tamiflu) (pp 1321, 1330, 1342, 1348, 1352, 1364). Between them the articles conclude that the evidence that oseltamivir reduces complications in otherwise healthy people with pandemic influenza is now uncertain and that we need a radical change in the rules on access to trial data.

Briefly, in updating their Cochrane review, published this week (p 1364), Tom Jefferson and colleagues failed to verify claims, based on an analysis of 10 drug company trials, that oseltamivir reduced the risk of complications in healthy adults with influenza. These claims have formed a key part of decisions to stockpile the drug and make it widely available.

Only after questions were put by the *BMJ* and *Channel 4 News* has the manufacturer Roche committed to making "full study reports" available on a password protected site. Some questions remain about who did what in the Roche trials, how patients were recruited, and why some neuropsychiatric adverse events were not reported. A response from Roche is published in our letters pages (p 1330) and their full point by point response is published online (doi:10.1136/bmj.b5374).

Should the *BMJ* be publishing the Cochrane review given that a more complete analysis of the evidence may be possible in the next few months? Yes, because Cochrane reviews are by their nature interim rather than definitive. They exist in the present tense, always to be superseded by the next update. They are based on the best information available to the reviewers at the time they complete

their review. The Cochrane reviewers have told the *BMJ* that they will update their review to incorporate eight unpublished Roche trials when they are provided with individual patient data.

Where does this leave oseltamivir, on which governments around the world have spent billions of pounds? The papers in this week's journal relate only to its use in healthy adults with influenza. They say nothing about its use in patients judged to be at high risk of complications—pregnant women, children under 5, and those with underlying medical conditions; and uncertainty over its role in reducing complications in healthy adults still leaves it as a useful drug for reducing the duration of symptoms. However, as Peter Doshi points out (p 1348), on this outcome it has yet to be compared in head to head trials with non-steroidal inflammatory drugs or paracetamol. And given the drug's known side effects, the risk-benefit profile shifts considerably if we are talking only in terms of symptom relief.

We don't know yet whether this episode will turn out to be a decisive battle or merely a skirmish in the fight for greater transparency in drug evaluation. But it is a legitimate scientific concern that data used to support important health policy strategies are held only by a commercial organisation and have not been subject to full external scrutiny and review. It can't be right that the public should have to rely on detective work by academics and journalists to patch together the evidence for such a widely prescribed drug. Individual patient data from all trials of drugs should be readily available for scientific scrutiny.

**Fiona Godlee, editor, *BMJ* fgodlee@bmj.com**

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**PLUS** Career Focus, jobs, and courses appear after p 1382

## WHAT'S NEW ON BMJ.COM

**SURVIVORS OF CHILDHOOD CANCERS**

According to this analysis of the Childhood Cancer Survivor Study cohort, survivors of childhood and adolescent cancer are at substantial risk for cardiovascular disease. Healthcare professionals must be aware of these risks when caring for this growing population. In the accompanying editorial, Meriel Jenney and Gill Levitt say that numbers of childhood cancer survivors are increasing, so a network of specialists that crosses age boundaries is needed.

Read this and more research at <http://www.bmj.com/channels/research.dtl>

**LATEST ON SWINE FLU**

Listen to the free BMJ Learning audio module with chief medical officer Sir Liam Donaldson answering doctors' questions about swine flu. Hear how to prioritise, whom to vaccinate, and the rationale behind the national guidelines. This interview was recorded on 25 November.

Click on the link: <http://learning.bmj.com/learning/search-result.html?moduleId=10013823>

**LATEST BLOGS**

Emily Spry is finding things tough in Freetown, Sierra Leone. She says, "Everyone warned me about this moment; when Freetown suddenly gets to you and you find that actually it's all too much," she writes "The dirt, the traffic, the open drains, the strangeness, the constant attention from strangers, the light and water going off, the desperate poverty, the malnourished, the needlessly sick and dying."

Tony Waterston and Frances Mortimer blog about an event last weekend that was a feeder event to the massive march to Parliament Square on climate change. "The Wave was set up to influence the negotiators heading this week to Copenhagen for the crucial UN talks—and certainly they did, as our climate minister was on the march and our health delegation spent 15 minutes questioning him at the roadside." Elsewhere David Pencheon, one of the speakers at The Wave, posts his speech.

Read this and other blogs at <http://blogs.bmj.com/bmj/>

**LATEST VIDEO****Maisie and George and the future of their planet**

In the UK, up to 25% of public sector emissions come from the NHS. To mark the Copenhagen climate change summit, the *BMJ* has commissioned a short video about how the health service can reduce its carbon footprint.

View this video and others at <http://www.bmj.com/video/>

**Last week's poll asked:**

**"Is the conflict of interest unacceptable when drug companies conduct trials on their own drugs?"**

**You voted:**

**No: 133 (25%)**

**Yes: 400 (75%)**

**This week's poll asks:**

**"Would you publicly confess to a serious mistake if you thought others could learn from your experience?"**

Cast your vote at <http://www.bmj.com/#poll-daddy-head>



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