

THIS WEEK

Articles in this print journal have already been published on thebmj.com and may have been shortened. Full versions with references and competing interests are on thebmj.com



p4

NEWS & VIEWS

- 1 News and research news
- 6 BMJ Confidential: Jane Dacre

FEATURES

- 14 **COVER** No correction, no retraction, no apology, no comment: paroxetine trial reanalysis raises questions about institutional responsibility
Peter Doshi
● EDITORIAL, p 10
● RESEARCH, p 11

ANALYSIS

- 17 **COVER** Evidence about electronic cigarettes: a foundation built on rock or sand?
Martin McKee and Simon Capewell

VIEWS

- 20 Letters
- 22 Observations
- 23 Margaret McCartney, Blog
- 24 Personal view
- 25 Obituaries



p7

EDITORIALS

- 7 **COVER** Time to question the NHS diabetes prevention programme
Public Health England's focus on individual behaviour change is unlikely to stem the epidemic of type 2 diabetes
Eleanor Barry et al
- 8 **COVER** Dietary fats, health, and inequalities
There's nothing good about trans fats; a total ban would be best for public health
J Lennert Veerman
● RESEARCH, p 12
- 9 Deficiencies in services for acute upper GI bleeding
Patients need rapid access to specialist care round the clock
Alan J Lobo et al
- 10 Liberating the data from clinical trials
Liberated trial data have enduring potential to benefit patients, prevent harm, and correct misleading research
David Henry and Tiffany Fitzpatrick



p12

RESEARCH

- 11 Restoring Study 329: efficacy and harms of paroxetine and imipramine in treatment of major depression in adolescence
Joanna Le Noury et al
● EDITORIAL, p 10
● FEATURE, p 14
- 12 **COVER** Potential of trans fats policies to reduce socioeconomic inequalities in mortality from coronary heart disease in England: cost effectiveness modelling study
Kirk Allen et al
● EDITORIAL, p 8
- 13 Exercise capacity and muscle strength and risk of vascular disease and arrhythmia in 1.1 million young Swedish men: cohort study
Kasper Andersen et al



p36

EDUCATION

CLINICAL REVIEW

- 27 Dengue fever
Senanayake A M Kularatne
● thebmj.com 1 CPD/CME hour

PRACTICE

PRACTICE POINTER

- 32 **COVER** Assessment and management of facial nerve palsy
Liam Masterson et al
● thebmj.com 0.5 CPD/CME hour
- 35 Endgames
- 36 Minerva

BMJ CAREERS

News: Consultants must not become scapegoats • Doctors need support, not resilience training • Why bother with a substantive post?
Followed by jobs and courses



Study 329
● pp 10, 11, 14

The BMA grants editorial freedom to the Editor of *The BMJ*. The views expressed in the journal are those of the authors and may not necessarily comply with BMA policy. *The BMJ* follows guidelines on editorial independence produced by the World Association of Medical Editors (www.wame.org/wamestmt.htm#independence) and the code on good publication practice produced by the Committee on Publication Ethics (www.publicationethics.org.uk/guidelines/). *The BMJ* is intended for medical professionals and is provided without warranty, express or implied. Statements in the journal are the responsibility of their authors and advertisers and not authors' institutions, the BMJ Publishing Group, or the BMA unless otherwise specified or determined by law. Acceptance of advertising does not imply endorsement. To the fullest extent permitted by law, the BMJ Publishing Group shall not be liable for any loss, injury, or damage resulting from the use of *The BMJ* or any information in it whether based on contract, tort, or otherwise. Readers are advised to verify any information they choose to rely on.

©BMJ Publishing Group Ltd 2015 All Rights Reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted in any form or by any other means, electronic, mechanical, photocopying, recording, or otherwise, without prior permission, in writing, of *The BMJ*. The BMJ, ISSN 1759-2151, is published weekly by BMJ Publishing Group Ltd, BMA House, Tavistock Square, London WC1H 9JR, UK. The US annual subscription price is \$1,660. Airfreight and mailing in the USA by agent named Worldnet Shipping Inc., 156-15, 146th Avenue, 2nd Floor, Jamaica, NY 11434, USA. Periodicals postage paid at Jamaica NY 11431. US Postmaster: Send address changes to *The BMJ*, Worldnet Shipping Inc., 156-15, 146th Avenue, 2nd Floor, Jamaica, NY 11434, USA. Subscription records are maintained at BMJ Publishing Group Ltd, BMA House, Tavistock Square, London WC1H 9JR, UK. Air Business Ltd is acting as our mailing agent. Printed by Polestar Limited.



thebmj

19 September 2015 Vol 351

The Editor, *The BMJ*
BMA House, Tavistock Square,
London WC1H 9JR

Email: editor@bmj.com
Tel: +44 (0)20 7387 4410
Fax: +44 (0)20 7383 6418

BMA MEMBERS' ENQUIRIES
Email: membership@bma.org.uk
Tel: +44 (0)20 7383 6955

BMJ CAREERS ADVERTISING
Email: sales@bmjcareers.com
Tel: +44 (0)20 7383 6531

DISPLAY ADVERTISING
Email: sales@bmjgroup.com
Tel: +44 (0)20 7383 6386

REPRINTS
UK/Rest of world
Email: ngurneyrandall@bmjgroup.com
Tel: +44 (0)20 8445 5825

USA
Email: mfogler@medicalreprints.com
Tel: +1 (856) 489 4446

SUBSCRIPTIONS
BMA Members
Email: membership@bma.org.uk
Tel: +44 (0)20 7383 6955
Non-BMA Members
Email: support@bmjgroup.com
Tel: +44 (0)20 7111 1105

OTHER RESOURCES
For all other contacts:
resources.bmj.com/bmj/contact-us
For advice to authors:
resources.bmj.com/bmj/authors
To submit an article:
submit.bmj.com

The BMJ is published by BMJ Publishing Group Ltd, a wholly owned subsidiary of the British Medical Association.

INDEXING THE BMJ
The BMJ is an online journal and we therefore recommend that you index content from thebmj.com rather than this print edition. We suggest you use the Digital Object Identifier (doi) available online at the top of every article.

All BMJ titles are produced with paper supplied from sustainable sources



PHILIPP GUELLAND/GETTY

PICTURE OF THE WEEK

Pictograms and Arabic writing on a makeshift sign show the way to a rest area and medical treatment in an emergency shelter for refugees on 14 September 2015 at the railway station in Salzburg, Austria. German authorities announced that they were temporarily reinstating controls along Germany's border with Austria in order to stem the recent influx of migrants

• [thebmj.com](http://www.bmj.com) Feature, *BMJ* 2015;351:h4881

THEBMJ.COM POLLS

Last week's poll asked:

Do we need more men in medicine

YES: 351 (51%) NO: 341 (49%)

Total votes: 692

• <http://www.bmj.com/content/351/bmj.h4646/rr-1>

This week's poll:

Was Public Health England right to endorse electronic cigarettes as a smoking cessation aid?

• <http://www.bmj.com/content/351/bmj.h4863>



*Mirabegron is recommended by NICE as an option for treating the symptoms of overactive bladder only for people in whom antimuscarinic drugs are contraindicated or clinically ineffective, or have unacceptable side effects.

Please consult the Summary of Product Characteristics before prescribing, particularly in relation to side-effects, precautions and contraindications. Further information is available on request from the product licence holder: Astellas Pharma Ltd, 2000 Hillwood Drive, Chertsey, Surrey, KT16 0RS, UK. Legal Category: POM. Information about this product, including adverse reactions, precautions, contraindications and method of use can be found at <http://www.medicines.org.uk/emc>

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard Adverse events should also be reported to Astellas Pharma Ltd. Please contact 0800 783 5018

Date of preparation: March 2015. BET15037UK.

 **Betmiga**TM
mirabegron

A fresh start in OAB

Accepted for use by the NICE

NICE recommended treatment option*

IT'S TIME TO THINK OF SOMETHING ELSE.

For the symptomatic treatment of urgency, increased micturition frequency and/or urgency incontinence as may occur in adult patients with overactive bladder (OAB) syndrome.

Online highlights from thebmj.com

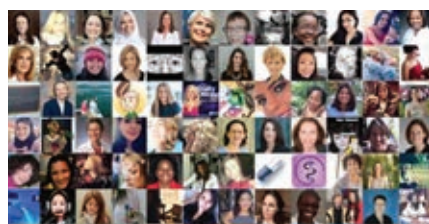
RESPONSE OF THE WEEK

E-cigarettes may be free from the toxins and carcinogens that cause lung cancer and other lung diseases but still contain nicotine and are harmful. Nicotine is not only addictive but also associated with peptic ulceration, coronary thrombosis, stroke, and peripheral vascular disease. From my 16 years of working as a surgeon in India I have memories of doing many lumbar sympathectomies and leg amputations for ischaemia in patients with Buerger's disease as a result of nicotine from the smoking of beedis. Surely these dangers make a case for total quitting and certainly not for the increasing availability of e-cigarettes.

Frank I Tovey, retired consultant surgeon, Lymington, UK, in response to, "Fuming about e-cigarettes and harm"

• [BMJ 2015;351:h4634](http://dx.doi.org/10.1136/bmj.2015.351.h4634)

OVERHEARD ON TWITTER



@DrEdFitzgerald

#ILookLikeASurgeon made it into *The BMJ* this week. Read our @bmj_latest blog on how it started <http://bmj.co/ILookLikeASurgeon>

@ThomIPhillips

Seen @bmj_latest? Data show that CVD and oncology patients are LESS likely to die at the weekend, especially Sunday! #weneedtotalkaboutjeremy

@Trisha_the_doc

So many of my heroes featuring in this week's @bmj_latest, not least the obituary for Oliver Sacks.



Twitter @bmj_latest

POPULAR ONLINE

Intake of saturated and trans unsaturated fatty acids and risk of all cause mortality, cardiovascular disease, and type 2 diabetes: systematic review and meta-analysis of observational studies

• [BMJ 2015;351:h3978](http://dx.doi.org/10.1136/bmj.2015.351.h3978)

Mental illness, challenging behaviour, and psychotropic drug prescribing in people with intellectual disability: UK population based cohort study

• [BMJ 2015;351:h4326](http://dx.doi.org/10.1136/bmj.2015.351.h4326)



Increased mortality associated with weekend hospital admission: a case for expanded seven day services?

• [BMJ 2015;351:h4596](http://dx.doi.org/10.1136/bmj.2015.351.h4596)

LATEST BLOGS

Delivering women centred care in maternity services

Do maternity services put women at the centre of care? Are medical professionals providing women with the necessary resources, choices, and information to have a positive birthing experience? Florence Smith, an NHS maternity support worker, reports on a recent conference that looked at how women centred care should be the practice and the norm.

• <http://bmj.co/NHSmaternity>



The puzzle of co-production with patients

Given that most people agree that co-production with patients is a good thing, why doesn't it happen more often? Ceinwen Giles set about trying to answer this question. She discovered that very few people truly understand what co-production means, and even fewer truly attempt it because it requires a change of culture and is something that challenges the dynamics between clinicians, managers, and patients.

• <http://bmj.co/co-production>

Global health and altruism

The past 10 years have not been easy for refugees hoping for sanctuary in Canada, writes Chris Simms, who says this is part of a wider government strategy, which has also seen Canada's social safety net significantly weakened. He cites research that shows rich countries that are less charitable to vulnerable populations at home also give less aid to poorer countries, and hopes for the sake of those at home and abroad that governments can show more generosity.

• http://bmj.co/global_health_altruism

Why is it hard to do the right thing?

When he's faced with a patient who complains of being tired, GP Samir Dawlatly finds himself at one of those crossroads that occur regularly in primary care: the choice to investigate what may be medicalised symptoms or do nothing. He describes how making this decision is made all the more difficult by all the other barriers to good care that practising GPs have to overcome.

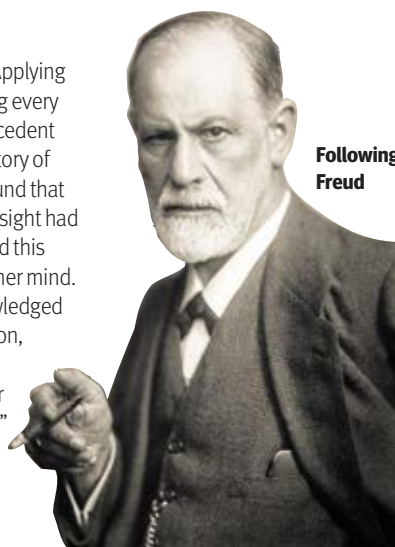
• http://bmj.co/right_thing_hard

THIS WEEK IN 1915

Dr Kenneth Campbell, surgeon to the Western Ophthalmic Hospital, writes about a case of hysterical amblyopia. The patient was a 21 year old woman whose visual acuity varied within wide limits—sometimes as low as 1/60, sometimes as high as 6/6. There was no element of malingering, no signs of disease, her blood pressure was not raised, and her urine was free from albumin. She did, however, exhibit classical symptoms of hysteria—she was emotional, self conscious, had poor will power, spoke in a whisper, and her life

had no satisfying aims. Applying Freud's method of tracing every symptom to "some antecedent experience in the life history of the individual," it was found that the patient's father's eyesight had recently begun to fail, and this preyed considerably on her mind. Once the patient acknowledged the source of her condition, and brought the "entire circumstances of it under the criticism of the mind," a cure was effected within nine months.

• Cite this as *BMJ* 1915;2:434



Following Freud

EDITOR'S CHOICE

Study 329

The restorative authors concluded that there is no advantage of paroxetine or imipramine over placebo

This week we release our first “RIAT” reanalysis of a previously published randomised trial (p 11). Avid readers will remember that RIAT stands for “restoring invisible and abandoned trials.” As described by its originators in 2013 (doi: 10.1136/bmj.f2865), it provides a mechanism for researchers unaffiliated with the original trial to publish unpublished (or to republish misreported) clinical trials when sponsors and original investigators fail to do so.

Last year Tom Treasure and colleagues reported a trial whose data had remained unpublished for 20 years (doi: 10.1136/bmjopen-2013-004385). In a narrative article in *The BMJ* the restorative authors said that the data cast doubt on the now common practice of carcinoembryonic antigen testing and metastasectomy in people with colorectal cancer (doi: 10.1136/bmj.g2085).

We expect many other trials to fall within RIAT’s purview. However, when RIAT was first conceptualised, I and others had one specific trial in mind. Study 329 was a placebo controlled randomised trial of paroxetine and imipramine in adolescents with major depression. As originally reported in 2001, it concluded that paroxetine was “generally well tolerated and effective.”

Paroxetine has never been approved for use in children, but as Peter Doshi reports (p 14), millions of off-label prescriptions later, Study 329 has become infamous. Funded by the manufacturer of paroxetine, SmithKline Beecham, now GSK, it was quickly dubbed by the US Food and Drug Administration a “failed trial,” as neither treatment was found to be better than placebo. We learnt that the paper was drafted not by

any of the 22 listed authors but by a writer paid by the manufacturer. But most alarmingly, reports emerged of serious adverse effects of paroxetine in adolescents, including self harm and suicidal ideation. In 2012 the US Department of Justice, investigating a failure to report safety data and other misconduct by GSK, settled criminal and civil proceedings with a record \$3bn fine. Efforts to get the authors, the journal that published the trial, the professional society that publishes the journal, and the authors’ institutions to act or even respond to criticism have failed.

Given this history, there was little doubt that the study needed restoration. That the original authors chose not to do this came as little surprise. The restorative authors set to work accessing and analysing the clinical study report and patient level data. From this immense task they concluded that there is no advantage of paroxetine or imipramine over placebo. They also uncovered “serious, severe, and suicide related adverse events” that had been overlooked or hidden.

The RIAT re-analysis marks a new chapter in the story of Study 329, showing the remarkable power of open data. But it also shows how much our current systems are failing patients and the public. It should not have taken 14 years to get to this point. It shows that we need regulation, and perhaps legislation, to ensure that the results of all clinical trials are made publicly available and that individual patient data are available for legitimate independent third party scrutiny.

Fiona Godlee, editor in chief, *The BMJ*
fgodlee@bmj.com

Cite this as: *BMJ* 2015;351:h4973

Twitter

Follow the editor, Fiona Godlee @fgodlee, and *The BMJ* at twitter.com/bmj_latest




Be kept up to date with the latest developments in health care and interact with other medical professionals.

www.facebook.com/thebmjdotcom

Join our Facebook community