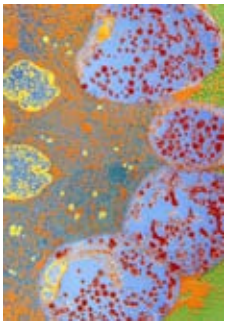
RESEARCH

The *BMJ* is an Open Access journal. We set no word limits on *BMJ* research articles, but they are abridged for print. The full text of each *BMJ* research article is freely available on bmj.com

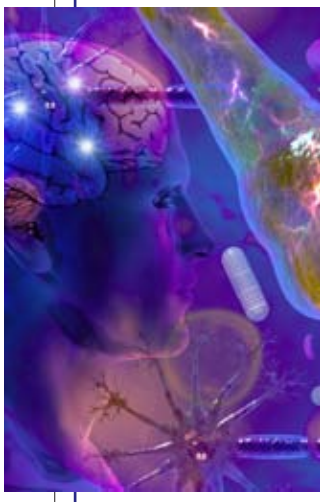


DR R DOURMASKIN/SPL

WHAT OUR READERS ARE SAYING

Two research papers in this week's *BMJ* have already attracted rapid responses on bmj.com.

Let us know what you think by submitting your own response



CAROL AND MIKE WERNER/VISUALS UNLIMITED INC/SPL

Cardiovascular safety of central nervous system stimulants in children and adolescents: population based cohort study
All respondents so far objected to using stimulants except as a method of last resort or in combination with other measures. "Exposure to one drug of abuse will prime a person for abuse of other drugs, creating a vulnerability that may persist for years and may lead to relapse," writes one, concluding: "Giving children dopaminergic drugs risks promoting addictive, high seeking behaviour in later life." "Psychotropics in children and adolescents is bad practice. It interferes with the normal development of sensitive, developing nervous systems, and invites iatrogenic conditions," writes another. "As long as it is remembered that medication alone is not enough for treatment of ADHD. It requires school support also (teachers, guidance counsellors) and psychological support for child and parents," writes a third.

Reoperation rates after breast conserving surgery for breast cancer among women in England: retrospective study of hospital episode statistics
Two breast specialists from Edinburgh write: "The problem in breast conserving surgery is not so much the variation in repeat excision rates highlighted in the *BMJ* report but the inconsistency in applying the current knowledge base on margin width. As stated by the authors, interpreting repeat excision rates without knowledge of local protocols as indicators of quality cannot be justified, yet that is the message that percolated to the media. As Morrow and colleagues argue in a recent article, surgeons need to abandon local protocols as suggested by the Association of Breast Surgeons and follow the evidence."

RESEARCH ONLINE: For these and other new research articles see bmj.com/research

Iatrogenic Cushing's syndrome and cardiovascular events
In this cohort study, the risk of cardiovascular events in people treated with glucocorticoids was nearly three times greater in those who develop iatrogenic Cushing's syndrome. People who use glucocorticoids and exhibit iatrogenic Cushing's syndrome should be aggressively targeted for early screening and management of cardiovascular risk factors, say the authors.

Association between psychological distress and mortality
In this individual participant pooled analysis of 10 large prospective cohort studies from the Health Survey for England, psychological distress was associated with increased risk of mortality from several major causes in a dose-response pattern. Risk of mortality was raised even at lower levels of distress. The authors advocate research into whether treatment can modify this increased risk.

Screening for colorectal cancer and advanced colorectal neoplasia in recipients of kidney transplants
This cross sectional prevalence and diagnostic accuracy study of faecal immunochemical testing for haemoglobin and colonoscopy included 229 kidney transplant recipients aged 50 years and older. The researchers found that the prevalence of advanced colorectal neoplasia in this group was 13% (29 cases). Faecal haemoglobin screening for colorectal neoplasia has similar performance characteristics in transplant recipients to those reported in general population studies, with poor sensitivity but reasonable specificity. Surveillance colonoscopy might be a more appropriate approach in this population than faecal haemoglobin testing, the authors concluded.

JAMES KING-HOLMES/SPL

Effectiveness of yearly, register based screening for chlamydia in the Netherlands: controlled trial with randomised stepped wedge implementation

Ingrid V F van den Broek,[1] Jan E A M van Bergen,[2 3] Elfi E H G Brouwers,[4] Johannes S A Fennema,[5] Hannelore M Götz,[6] Christian J P A Hoebe,[4] Rik H Koekenbier,[5] Mirjam Kretzschmar,[1 7] Eelco A B Over,[8] Boris V Schmid,[1] Lydia L Pars,[3] Sander M van Ravesteijn,[9] Marianne A B van der Sande,[1 7] G Ardine de Wit,[7 8] Nicola Low,[10] Eline L M Op de Coul[1]

EDITORIAL by Andersen and Olesen

[1]Unit of Epidemiology and Surveillance, RIVM/Centre for Infectious Disease Control Netherlands, PO Box 1, 3720 BA Bilthoven, Netherlands
[2]University of Amsterdam, 1012 WX Amsterdam, Netherlands
[3]STI AIDS Netherlands, Keizersgracht 390, 1016 GB Amsterdam, Netherlands
[4]South Limburg Public Health Service, PO Box 2022, 6160 HA Geleen, Netherlands
[5]Amsterdam Public Health Service, Nieuwe Achtergracht 100, 1018 WT Amsterdam, Netherlands
[6]Department of Infectious Disease Control, Municipal Public Health Service Rotterdam-Rijnmond, PO Box 70032, 3000 LP Rotterdam, Netherlands
[7]Julius Centre for Health Sciences & Primary Care, University Medical Centre Utrecht, Heidelberglaan 100, 3584 CX Utrecht, Netherlands
[8]Centre for Prevention and Health Services Research, RIVM Netherlands. Bilthoven, Netherlands
[9]Municipal Public Health Service Rotterdam-Rijnmond, Schiedamsedijk 95, 3011 EN Rotterdam, Netherlands
[10]Institute of Social and Preventive Medicine, University of Bern, Finkenhubelweg 11, 3012 Bern, Switzerland
Correspondence to: I V F van den Broek
Ingrid.van.den.Broek@rivm.nl

Cite this as: *BMJ* 2012;345:e4316
doi: 10.1136/bmj.e4316

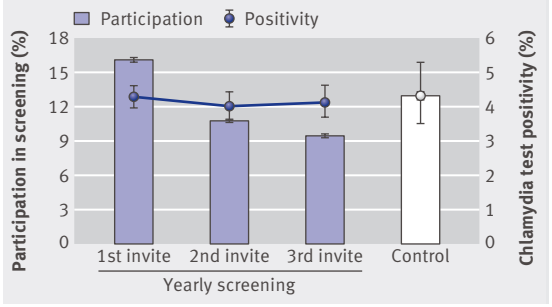
This is a summary of a paper that was published on bmj.com as *BMJ* 2012;345:e4316

STUDY QUESTION Does chlamydia screening, with yearly invitations, reach enough people to reduce prevalence of chlamydia infection in the population?

SUMMARY ANSWER There was no statistical evidence of an impact on chlamydia prevalence after three screening rounds, probably because of the low participation rates.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS
Chlamydia infection is a common sexually transmitted infection, and screening to detect and treat asymptomatic infections is widely practised. The effect of chlamydia screening on transmission at the population level has not been studied in randomised trials. This controlled trial found that multiple rounds of screening at population level had low participation and no significant effect on chlamydia positivity.

Participation in yearly chlamydia screening and test positivity compared with one-off control screening



Design
The intervention was a register based programme with personalised invitations to eligible people to be screened yearly for *Chlamydia trachomatis* for three years; invitees could request a kit for self sampling from a secure website. Invitations were sent to all eligible individuals in geographical clusters. De-identified clusters were assigned to intervention and control blocks to achieve groups balanced for expected community risk and cluster size. The intervention was implemented using a stepped wedge design, with sequential roll out in random order, including each cluster at least once. People in control clusters had access to usual care until their single screening invitation, which was sent after the second invitation in the intervention group.

Participants and setting
The trial ran from March 2008 to February 2011. The target group was all women and men aged 16-29 years during the trial period listed in municipal registers in three regions in the Netherlands (two urban and one suburban and rural area). The total target population was 315 000 divided among 190 clusters, of which 39 were in the control group.

Primary outcome(s)
Chlamydia test positivity among participants, percentage participating, and estimated prevalence of infection.

Main results and the role of chance
A total of 102 283 people were tested for chlamydia, and 4252 infections detected. Participation in the intervention group was 16.1% at the first invitation, 10.8% at the second, and 9.5% at the third. In the control group, 13.0% took part. The initial chlamydia test positivity was 4.3% among participants in both intervention and control groups (figure). There was no measurable impact on positivity when comparing the intervention group at the third invitation with the control group (odds ratio 0.96 (95% CI 0.83 to 1.10), P=0.5). The results did not change after controlling for baseline differences in cluster allocation, community risk, and cluster size. In the small group that participated three times (n=4510, 2.8% of invitees), test positivity fell from 5.9% to 2.9% (odds ratio 0.49 (0.47 to 0.50)). Chlamydia prevalence could not be measured accurately because of low levels of screening uptake.

Harms We did not measure harms.

Bias, confounding, and other reasons for caution
Selection bias might have occurred because of the non-random allocation of clusters to intervention and control groups. We do not think this affected the results because these did not change after controlling for baseline differences. The effect of screening on chlamydia positivity might have been diluted by mixing between sexual networks in unscreened and screened areas and by the level of opportunistic chlamydia testing in usual care. About 10-12% of young adults in the Netherlands get tested each year for sexually transmitted infections in general practice or specialist clinics.

Generalisability to other populations
The results can be generalised to populations where opportunistic chlamydia testing is freely available in healthcare settings and where population registers are used for screening programmes.

Trial registration number
NTR 3071 (Netherlands Trial Register).

Clopidogrel and interaction with proton pump inhibitors: comparison between cohort and within person study designs

Ian J Douglas,[1] Stephen J W Evans,[1] Aroon D Hingorani,[2] Anthony M Grosso,[3] Adam Timmis,[4] Harry Hemingway,[2] Liam Smeeth[1]

EDITORIAL by Targownik

[1]Faculty of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, London WC1E 7HT, UK
[2]Department of Epidemiology and Public Health, University College London, London WC1E 6BT
[3]Pharmacy Department, University College London Hospital, London NW1 2PG
[4]Department of Cardiology, Barts and The London Heart and Chest Centre, London E2 9JX
Correspondence to: I J Douglas
ian.douglas@lshtm.ac.uk

Cite this as: *BMJ* 2012;345:e4388
doi: 10.1136/bmj.e4388

This is a summary of a paper that was published on bmj.com as *BMJ* 2012;345:e4388

STUDY QUESTION Does the pharmacokinetic interaction between proton pump inhibitors and clopidogrel lead to harmful vascular events?

SUMMARY ANSWER The addition of a proton pump inhibitor to clopidogrel and aspirin does not seem to cause clinical harm. Associations between use of proton pump inhibitors and harmful outcomes are probably because of fundamental differences between users and non-users of proton pump inhibitors because no harm is detected when comparisons are made within people, with each participant acting as his or her own control.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Studies examining whether the pharmacokinetic interaction between clopidogrel and proton pump inhibitors leads to vascular harm have had conflicting results. We have shown that apparent harmful outcomes associated with use of a proton pump inhibitor might be caused by differences between patients prescribed and not prescribed a proton pump inhibitor rather than a reduction in the effectiveness of clopidogrel.

Participants and setting

Participants were all receiving prescribed clopidogrel and aspirin, registered in the United Kingdom General Practice Research Database, and linked with the Myocardial Ischaemia National Audit Project (MINAP) between 1 January 2003 and 31 July 2009.

Design, size, and duration

We included 24 471 people receiving clopidogrel and aspirin, with 12 439 additionally receiving a proton pump inhibitor during their follow-up period (median follow-up about one year). We carried out a cohort analysis for the outcomes of all cause mortality or myocardial infarction, all cause mortality, myocardial infarction, vascular mortality, and non-vascular mortality. A self controlled case series was conducted for the outcome of myocardial infarction. Additional exposures included for comparison were other inhibitors of the CYP450 2C19 enzyme (including strong inhibitors such as omeprazole, esomeprazole, lansoprazole) and weak inhibitors or non-inhibitors (such as citalopram and ranitidine).

Main results and the role of chance

Death or incident myocardial infarction occurred in 1419 (11%) patients while they were receiving a proton pump inhibitor compared with 1341 (8%) who were not receiving a proton pump inhibitor. The adjusted hazard ratio for the association between proton pump inhibitor use and death or incident myocardial infarction was 1.37 (95% confidence interval 1.27 to 1.48). Comparable results were seen for secondary outcomes and with other 2C19 inhibitors and with non-inhibitors. With the self controlled case series design to remove the effect of differences between people, we found no association between proton pump inhibitor use and myocardial infarction, with a rate ratio of 0.75 (0.55 to 1.01). Similarly, there was no association with myocardial infarction for other drugs studied.

Bias, confounding, and other reasons for caution

We accounted for potential confounders in the cohort analysis but might not have been able to entirely account for differences between people, which we believe can explain the association between proton pump inhibitors and harmful outcomes. Drug exposure might have been misclassified to some extent as it was based on prescribing rather than consumption. The most likely effect of this would be to bias results towards the null.

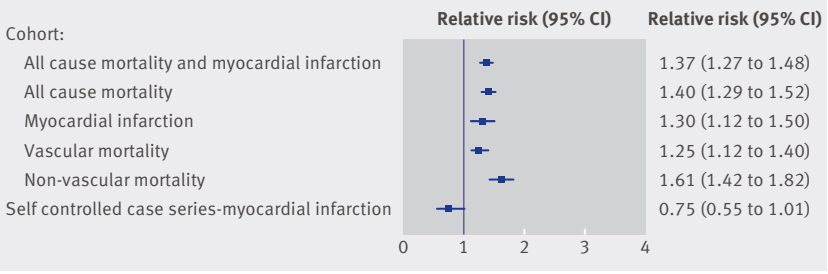
Generalisability to other populations

The study was population based and results are probably generalisable to other populations.

Study funding/potential competing interests

IJD is funded by a Medical Research Council Methodology Fellowship and LS is funded by a Wellcome Trust Fellowship. AT acknowledges the support of Barts Cardiovascular Biomedical Research Unit funded by the National Institute for Health Research. IJD consults for GlaxoSmithKline, Takeda, and Gilead, and holds stock in GlaxoSmithKline; LS consults for GlaxoSmithKline.

Association between exposure to proton pump inhibitors and outcomes in cohort analysis (hazard ratio) and self controlled case series (incidence rate ratio) in patients taking clopidogrel and aspirin



bmj.com

- Clinical Review: Clopidogrel in acute coronary syndromes (*BMJ* 2009;338:b1180)
- Research: Ticagrelor versus clopidogrel in patients with acute coronary syndromes intended for non-invasive management (*BMJ* 2011;342:d3527)
- Research: Impact of CYP2C19 variant genotypes on clinical efficacy of antiplatelet treatment with clopidogrel (*BMJ* 2011;343:d4588)

Cardiovascular safety of central nervous system stimulants in children and adolescents: population based cohort study

Almut G Winterstein,[1 2] Tobias Gerhard,[3] Paul Kubilis,[1] Arwa Saidi,[4] Stephan Linden,[1] Stephen Crystal,[5] Julie Zito,[6] Jonathan J Shuster,[7] Mark Olfson[8]

[1]Pharmaceutical Outcomes and Policy, College of Pharmacy, University of Florida, Gainesville, FL 32611, USA
[2]Epidemiology, Colleges of Medicine and Public Health and Health Profession, University of Florida, Gainesville, FL
[3]Ernest Mario School of Pharmacy and Institute for Health, Health Care Policy, and Aging Research, Rutgers, State University of New Jersey, New Brunswick, NJ 08901, USA
[4]Pediatric Cardiology, College of Medicine, University of Florida, Gainesville, FL
[5]Center for Health Services Research on Pharmacotherapy, Chronic Disease Management, and Outcomes, Rutgers University, New Brunswick, NJ
[6]University of Maryland, Baltimore, MD 21201, USA
[7]Department of Health Outcomes and Policy, UF Clinical Research Center, College of Medicine, University of Florida, Gainesville, FL
[8]Department of Psychiatry, Columbia University, New York State Psychiatric Institute, New York, NY 10032, USA
Correspondence to: A G Winterstein
almut@cop.ufl.edu

Cite this as: *BMJ* 2012;345:e4627
doi: 10.1136/bmj.e4627

This is a summary of a paper that was published on bmj.com as *BMJ* 2012;345:e4627

bmj.com
Cardiology updates from BMJ Group at http://bit.ly/MnSoOq

STUDY QUESTION Is the use of central nervous stimulants in children with mental health conditions such as attention-deficit/hyperactivity disorder associated with an increased risk of serious cardiac events?

SUMMARY ANSWER Treatment of children with stimulants is not significantly associated with an increase in the short term risk of serious cardiac events.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS Only one of several observational studies was sufficiently powered to investigate the risk for major cardiovascular events and found no association. In this more vulnerable population of children eligible for public insurance in the United States we found no significant association between the short term use of stimulants for the treatment of mental health conditions and the outcomes of stroke, acute myocardial infarction, or sudden cardiac death.

Unadjusted and adjusted incidence rates for sudden cardiac death, acute myocardial infarction, and stroke per 100 000 patient years associated with stimulant use in children and young people with mental health diagnosis

	Unadjusted	Adjusted*
Full cohort:		
Non-use	3.5 (2.7 to 4.6)	Reference
Current use	1.7 (0.8 to 3.5)	2.2 (1.0 to 5.1)
Former use	1.5 (0.7 to 3.4)	2.0 (0.8 to 4.9)
Low risk cohort:		
Non-use	2.1 (1.5 to 3.0)	Reference
Current use	1.0 (0.4 to 2.6)	1.0 (0.3 to 3.1)
Former use	1.3 (0.5 to 3.1)	1.5 (0.6 to 4.0)
High risk cohort:		
Non-use	75.2 (49.5 to 114.1)	Reference
Current use	51.5 (16.6 to 159.7)	76.7 (21.0 to 277.3)
Former use	17.0 (2.4 to 120.5)	24.1 (3.1 to 183.4)

*Calculated by multiplying crude event rate of non-users by respective adjusted odds ratios.

Participants and setting

We enrolled children and young people aged 3-18 with a diagnosis of a mental health condition commonly treated with stimulants (such as attention-deficit/hyperactivity disorder) and who were eligible for Medicaid. Exclusion criteria included transplant recipients, receipt of dialysis, or claims indicating substance misuse. For the stratified analysis we retained those at high risk who had similar use of stimulants to those at low risk (such as children with congenital heart disease).

Design, size, and duration

In this population based retrospective cohort study we used discrete survival analysis to estimate the relative risk for periods of stimulant use and non-use, adjusted for propensity score (summarising sociodemographic characteristics, cardiac risk factors, and psychiatric diagnoses obtained from before the index period) and use of antipsychotics. The mean and median follow-up time for the whole cohort was 1.9 years and 1.6 years, respectively.

Main results and the role of chance

A total of 66 events occurred during 2 321 311 person years of follow-up. The adjusted odds ratio for current versus no stimulant use was 0.62 (95% confidence interval 0.27 to 1.44), with a corresponding adjusted incidence rate of 2.2 and 3.5 per 100 000 patient years, respectively. Twenty six events occurred in high risk patients (incidence rate 63 per 100 000 patient years) with an odds ratio of 1.02 (0.28 to 3.69). The upper confidence limit for the full cohort suggests that the maximum increase in risk should be no higher than 44%. While the point estimate for the high risk cohort also suggests no increase, the confidence intervals were wider.

Bias, confounding, and other reasons for caution

We might not have been able to capture the full range of cardiac risk factors from claims data, and stimulant users might have been generally healthier. We also cannot exclude non-adherence or illicit use of stimulants, which would result in misclassification of users and underestimate the risk of stimulants. We could not examine the safety of long term use of stimulants. Likewise, it is unclear whether the effect of even subtle increases in blood pressure or heart rate could manifest many years after use of stimulants. Finally, we could not provide comparative safety estimates for different doses of stimulants or for methylphenidate and mixed amphetamine salts separately, but, given the small overall incidence of severe cardiac events, differences are expected to be subtle.

Generalisability to other populations

Our cohort represents a vulnerable population of children eligible for public insurance in the US and might not be generalisable to other populations.

Study funding/potential competing interests

This study was funded by grant R01-HS0185606 from the Agency of Healthcare Research and Quality (AHRQ) and in part by NIH grant 1UL1 TR000064 from the National Center for Advancing Translational Sciences. MO has received funding from the National Institute for Mental Health for a related topic.

Validation of treatment strategies for enterohaemorrhagic *Escherichia coli* O104:H4 induced haemolytic uraemic syndrome: case-control study

Jan Menne,[1] Martin Nitschke,[2] Robert Stingele,[3] Jürgen Büning,[2] Mario Schiffer,[1] Tanja Kuehbacher,[3] on behalf of the EHEC-HUS consortium

EDITORIAL by Artunc

[1]Department of Nephrology and Hypertension, Medical School Hannover, Carl Neuberg Strasse 1, 30625 Hannover, Germany
[2]University Hospital Schleswig-Holstein, Lübeck, Germany
[3]University Hospital Schleswig-Holstein, Kiel, Germany
Correspondence to: J Menne
menne.jan@mh-hannover.de

Cite this as: *BMJ* 2012;345:e4565
doi: 10.1136/bmj.e4565

This is a summary of a paper that was published on bmj.com as *BMJ* 2012;345:e4565

STUDY QUESTION What are the effects of different treatment strategies such as plasmapheresis, plasmapheresis with glucocorticoids, antibiotics, and eculizumab on Shiga toxin induced haemolytic uraemic syndrome (HUS)?

SUMMARY ANSWER Contrary to previous assumptions we could not demonstrate a benefit of plasmapheresis, associated glucocorticoid therapy, or eculizumab. Antibiotic treatment is not harmful and might even be beneficial in patients with established HUS.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Owing to the sporadic nature of HUS most published studies examined the efficacy of treatment strategies in small groups and lacked a comparator. The large number of patients affected in the 2011 outbreak of enterohaemorrhagic *E coli* (EHEC) induced HUS and differences in treatments between the hospitals allowed us to compare and analyse treatment options in an exploratory fashion. We found no clear benefit of plasmapheresis, glucocorticoids, and eculizumab.

Participants and setting

We included 23 hospitals treating a total of 395 adults with EHEC induced HUS. 97 of these patients were excluded as they were part of an industry sponsored trial of eculizumab.

Main results and the role of chance

Of the remaining 298 patients, 160 (54%) temporarily required dialysis, but only three required long term treatment. 37 (12%) had seizures, 54 (18%) required mechanical ventilation, and 12 (4%) died. We found no clear benefit from plasmapheresis or plasmapheresis with glucocorticoids. 67 of the remaining 298 patients were treated with eculizumab. No short term benefit was detected that could be attributed to this treatment. 52 patients in a centre administering an aggressive strategy of combined antibiotics had fewer seizures (2% *v* 15%, P=0.03) and deaths (0% *v* 5%, P=0.029), required no abdominal surgery, and excreted EHEC for a shorter duration.

Bias, confounding, and other reasons for caution

Because of the non-randomised group assignments our comparators were imperfect controls and bias was introduced by indication. Also, differences between the centres owing to the industry sponsored trial give rise to bias. Whenever possible we adjusted analyses to take account of the differences in baseline severity of HUS.

Generalisability to other populations

Data gathered by German paediatricians suggest that the clinical course and outcome of the *E coli* O104:H4 induced disease is similar to infections with the more common *E coli* O157:H7 induced HUS. Therefore, data generated from the 2011 outbreak in Germany might add valuable information for the treatment of all patients with Shiga toxin induced HUS.

Study funding/potential competing interests

We had no support from any organisation for the submitted work or other relationships or activities that could appear to have influenced the submitted work.

Percentage of patients affected in centres using different treatment strategies

Variables	Limited plasmapheresis* *v* platelet guided plasmapheresis†	No treatment versus treatment	
		Pre-emptive antibiotics	Eculizumab‡
No per group	54 *v* 197	246 *v* 52	65 *v* 67
% with event (odds ratio):			
Dialysis	15 *v* 32 (3.30)**	52 *v* 64 (0.54)	82 *v* 76 (1.00)
Ventilation	4 *v* 16 (12.05)*	18 *v* 17 (0.38)	42 *v* 34 (0.58)
Seizure	9 *v* 10 (1.70)	15 *v* 2 (0.03)**	29 *v* 24 (2.28)
Death	6 *v* 3 (0.10)	5 *v* 0 (not estimable)§	8 *v* 5 (0.28)

*3-5 sessions.
†Treatment stopped when platelets were at least 100/nL. Only events after first plasmapheresis are counted.
‡Patients in control group matched for severity of disease in patients who received eculizumab.
§0% in one group.
*P<0.05, **P<0.01 versus control.

Reoperation rates after breast conserving surgery for breast cancer among women in England: retrospective study of hospital episode statistics

R Jeevan,[1] D A Cromwell,[1 2] M Trivella,[1 3] G Lawrence,[4] O Kearins,[4] J Pereira,[5] C Sheppard,[6] C M Caddy,[7] J H P van der Meulen[1 2]

[1]Clinical Effectiveness Unit, Royal College of Surgeons of England, London WC2A 3PE, UK
[2]Department of Health Services Research and Policy, London School of Hygiene and Tropical Medicine, 15-17 Tavistock Place, London WC1H 9SH
[3]UK Cochrane Centre, National Institute for Health Research, Oxford OX2 7LG, UK
[4]West Midlands Cancer Intelligence Unit, University of Birmingham, Birmingham B15 2TT, UK
[5]James Paget University Hospitals NHS Foundation Trust, Great Yarmouth NR31 6LA, UK
[6]Portsmouth Hospitals NHS Trust, Queen Alexandra Hospital, Portsmouth PO6 3LY, UK
[7]Sheffield Teaching Hospitals NHS Foundation Trust, Royal Hallamshire Hospital, Sheffield S10 2JF, UK
Correspondence to:
D Cromwell
david.cromwell@lshtm.ac.uk

Cite this as: *BMJ* 2012;345:e4505
doi: 10.1136/bmj.e4505

This is a summary of a paper that was published on bmj.com as *BMJ* 2012;345:e4505

bmj.com
Oncology updates from BMJ Group at http://bit.ly/MrRoPi

STUDY QUESTION What is the rate of reoperation among women having breast conserving surgery for breast cancer in England, and do reoperation rates vary among different patient groups and among NHS trusts?

SUMMARY ANSWER Overall, 20.0% of women had at least one reoperation, but the reoperation rate was 29.5% for women with a carcinoma in situ disease component, and reoperation rates varied substantially across English NHS trusts.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS More than half of the 45 000 women diagnosed as having breast cancer in England have breast conserving surgery. Reoperation rates varied substantially between NHS trusts, raising questions about the uniformity of the selection criteria for both primary breast conserving surgery and reoperation

Participants and setting

We used hospital episode statistics data to identify all adult women with breast cancer who had primary breast conserving surgery in English NHS trusts between 1 April 2005 and 31 March 2008.

Design, size, and duration

This retrospective cohort study analysed the data for 55 297 women to estimate rates of reoperation within three months of primary breast conserving surgery. We used logistic regression to adjust reoperation rates for type of tumour, age, comorbidity, and socioeconomic deprivation. We grouped tumours by whether a carcinoma in situ component was coded at the time of the primary breast conserving surgery.

Main results and the role of chance

Overall, 11 032 women (20%, 95% confidence interval 19.6% to 20.3%) had at least one reoperation. Of these, 10 212 (18.5%, 18.2% to 18.8%) had one reoperation only—5943 (10.7%, 10.5% to 11.0%) had another breast conserving procedure, and 4269 (7.7%, 7.5% to 8.9%) had a mastectomy. Of the 45 793 women with isolated invasive disease, 8229 (18.0%) women had at least one reoperation. In comparison, 2803 (29.5%) of the 9504 women with carcinoma in situ had at least one reoperation (adjusted odds ratio 1.9, 95% confidence interval 1.8 to 2.0). Adjusted reoperation rates varied substantially across English NHS trusts (10th and 90th centiles 12.2% and 30.2%).

Bias, confounding, and other reasons for caution

This analysis used an administrative NHS database. Hospital episode statistics do not include records of treatment in independent sector hospitals, and patients migrating between the NHS and independent sector could have lowered the estimated overall reoperation rate. Inaccuracies in coding of procedures could have affected population selection and identification of reoperations, but validation work suggests that hospital episode statistics capture breast cancer surgery accurately. The presence of carcinoma in situ disease was based on the definitive postoperative histology rather than preoperative histological diagnosis. The lack of information on potential confounders (such as lobular histology, location and size of tumour, and lymphovascular invasion) is likely to have reduced the discriminatory performance of the risk adjustment model.

Generalisability to other populations

The study's findings are generalisable to the United Kingdom. Reoperation after breast conserving surgery will occur in other countries, but the average rate may differ. Reoperation rates are likely to vary between providers within other countries, but the magnitude of this variation may not be similar to that observed between English NHS trusts.

Study funding/potential competing interests

This study was not commissioned. JHPvdM received a national public health career scientist award from the Department of Health and NHS research and development programme.

Patterns of breast reoperation within three months of primary breast conserving surgery, categorised by type of tumour

	Women without carcinoma in situ disease		Women with carcinoma in situ disease	
Patient group	No	% (95% CI)	No	% (95% CI)
Women who had breast conserving surgery	45 793		9504	
Women who had no reoperation	37 564	82.0 (81.7 to 82.4)	6701	70.5 (69.6 to 71.4)
Women who had one reoperation:				
Additional breast conserving operation	4441	9.7 (9.4 to 10.0)	1502	15.8 (15.1 to 16.6)
Mastectomy	3201	7.0 (6.8 to 7.2)	1068	11.2 (10.6 to 11.9)
Women who had two or more reoperations	587	1.3 (1.2 to 1.4)	233	2.5 (2.2 to 2.8)