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

RESEARCH

THIS WEEK'S RESEARCH QUESTIONS

Assessing workplace based assessment

For doctors, learning doesn't stop after medical school: they have to complete courses, take professional exams, and keep up to date with good medical practice throughout their careers. One contribution to continuing professional development is "workplace based assessments," in which a doctor's day to day clinical performance and competence are evaluated in context. However, it's fair to say that workplace based assessment is very time consuming and not very popular with either junior doctors or consultants.

MARK THOMAS/SPL

Perhaps those who struggle with these assessments should pay heed to Alice Miller and Julian Archer's research into how workplace based assessment affects physician education and performance (p 710). The authors conducted a systematic review of 16 studies, 15 of which were non-comparative descriptive or observational studies. They found that although most doctors considered that multisource feedback had educational value, there was little evidence that such feedback resulted in change in practice. However, doctors were more likely to report changing their practice when feedback was credible and accurate or when coaching was provided to help subjects identify their strengths and weaknesses.

Most notably, individual factors had a profound effect on the magnitude of doctors' response to feedback, indicating that perhaps trainers need to tailor their responses to trainees to get the best performance. However, elsewhere in this week's journal (see Analysis, p 706), T Horsley and colleagues argue that continuing professional development procedures like workplace based assessment should be more standardised, in particular across Europe.

Oseltamivir: another piece of the puzzle

FREDERIC J BROWN/GETTY

In 2009 pandemic influenza A(H1N1) virus spread rapidly, resulting in millions of cases and more than 18 000 deaths in over 200 countries. Despite governments around the world spending billions of pounds on antivirals, the extent to which these drugs benefit otherwise healthy individuals with a mild H1N1 infection remains unknown, although these people represent the reservoir from which infection is transmitted to others.

Hongjie Yu and colleagues reviewed the medical records of 1291 patients in China who had laboratory confirmed mild H1N1 infection during the 2009 pandemic (p 714). Using multivariable logistic regression they found that oseltamivir treatment was a significant protective factor against subsequent development of radiographic pneumonia. This protective effect was seen in all patients, including those who started treatment more than two days after onset of symptoms—an interesting finding in view of the drive to start treatment as early as possible during the pandemic. They also found that treatment started within two days reduced the duration of fever and RNA viral shedding, and that 2009 H1N1 might be shed longer than seasonal influenza virus.

The authors, however, stress that their findings should be interpreted with caution. The study had some flaws, including its retrospective design and the fact that not all patients underwent chest radiography. They call for continued investigation into the effectiveness of antiviral treatment "to allow for improvement both in clinical treatment and public health guidance."

It's a call we support. A Cochrane review (2009;339:b5106) and investigation (2009;339:b5387) published in the *BMJ* last year questioned the evidence for the effectiveness and safety of oseltamivir. The inquiry into why relevant data were not publicly available for review cast doubt on the processes by which the drug had been evaluated, regulated, and promoted (2009;339:b5351). The availability of new data will help to build a truer picture of the drug's capabilities, so we welcome new high quality studies on the effectiveness of oseltamivir. But the authors are right to be cautious—and questions still remain over the public availability of data about the drug. As with all *BMJ* research papers, we are making this study freely available online for further scrutiny.

LATEST RESEARCH: For these and other new research articles see http://www.bmj.com/channels/research.dtl

MARTIN ROEMERS/PANOS

Reducing cardiovascular risk through diet in India Circumstantial evidence indicates that poor diet in early life might increase a person's sensitivity to lifestyle related risk factors for cardiovascular disease. Sanjay Kinra and colleagues sought to clarify this hypothesis by following up mothers and their offspring in the south of India who took part in a community trial of nutritional supplementation in 1987-90 (doi:10.1136/bmj.a605). They found that improving the protein-calorie intake of pregnant women and young children as part of other public health programmes was associated with a more favourable profile of cardiovascular risk factors in adolescence. Given that this intervention was cheap and relatively easy to implement, this approach could be an important tool for primary prevention of cardiovascular diseases in low income and middle income countries.

Osteoarthritis: evidence into practice A poll by Journal Watch asked doctors whether the findings of Simon Wandel and colleagues' meta-analysis (p 711)—which indicated no benefit from chondroitin or glucosamine—would affect what they recommended to patients with osteoarthritis. Of 438 responders, 53% said they would stop recommending glucosamine and chondroitin to patients on the basis of this evidence; 27% said they'd keep recommending them; and 19% said the information was not applicable to their practice (http://features.jwatch.org/pfwPollArchive.aspx).

Impact of workplace based assessment on doctors' education and performance: a systematic review

Alice Miller, Julian Archer

EDITORIAL by Sandars
See also ANALYSIS, p 706

Peninsula College of Medicine and Dentistry, University of Plymouth, Plymouth PL4 8AA, UK
Correspondence to: A Miller
alice.miller@pms.ac.uk

Cite this as: *BMJ* 2010;341:c5064
doi: 10.1136/bmj.c5064

This is a summary of a paper that was published on bmj.com as *BMJ* 2010;341:c5064

STUDY QUESTION

What is the evidence that workplace based assessment affects doctors' education and performance?

SUMMARY ANSWER

Despite the emphasis placed on workplace based assessment as a method of formative performance assessment, there are few published articles exploring its impact on physician education and performance.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Workplace based assessment is assumed to support educational impact and learning. This review found little evidence for it as an educational initiative, although there is some limited evidence that multisource feedback may lead to performance improvement.

Selection criteria for studies

We identified studies of any design that attempted to evaluate the impact or effect of the four workplace based assessments in common use internationally (multisource feedback, mini-clinical evaluation exercise, direct observation of procedural skills, and case based discussion) on the performance of fully qualified medical practitioners. Review articles, commentaries, and letters were excluded. The primary data sources were Journals@Ovid, Medline, Embase, CINAHL, PsycINFO, and ERIC. Evidence based reviews (Bandolier, *Cochrane Library*, DARE, HTA Database, and NHS EED) were accessed and searched via the Health Information Resources website. We also searched reference lists of relevant studies and bibliographies of review articles.

Primary outcome(s)

We evaluated studies that attempted to explore either the educational impact or the effect of workplace based assessment on doctors' performance, using Barr's adaptation of Kirkpatrick's four level evaluation model (see table).

Main results and role of chance

We included 16 studies: 15 were non-comparative descriptive or observational studies, and one was a randomised controlled trial (table). Eight studies examined multisource feedback, with mixed results. Performance changes were more likely to occur when feedback was credible and accurate or when coaching was provided to help subjects identify their strengths and weaknesses. Four studies examined the mini-clinical evaluation exercise, one looked at direct observation of procedural skills, and three were concerned with multiple assessment methods: all of these studies reported positive results for the educational impact of the workplace based assessments, but there was insufficient evidence to show objective improvement in performance.

Bias, confounding, and other reasons for caution

Most of the articles included in this review were non-comparative descriptive or observational studies, and their quality was mixed. Strength of findings may be limited by the uncontrolled nature of the studies, but given the methodological difficulties of evaluating educational impact and doctor performance, descriptive and observational studies can still provide useful information. Indeed, some of the strongest evidence for improved performance after workplace based assessment comes from detailed focus group data. The single randomised controlled trial attempted to establish causality ("multisource feedback causes performance improvement"), but the confounding factors relating to concurrent coaching undoubtedly affected the results. Methodological rigour is apparent in some articles, especially those aiming to evaluate multiple facets of workplace based assessment, but, because their focus tended to be on reliability and feasibility, they were less suitable for gathering data about educational impact or performance change. The potential bias of highly motivated study populations can lead to profoundly skewed results. The reliance on self reporting and the small study populations in most of the studies also affect the quality and strength of findings.

Our review methodology has its limitations. The database search was extensive, but the grey literature was not reviewed, leading to a potential publication bias, and the Ovid database search was limited to the English language.

Study funding/potential competing interests

No funding was obtained, and the authors have no competing interests.

STUDIES OF EFFECTS OF WORKPLACE BASED ASSESSMENT ON DOCTORS' PERFORMANCE

No of studies and participants	Reported impact	Quality grading of studies	Overall level of evaluation*
Multisource feedback			
8 studies, 1992 participants	Self reported positive changes in attitudes and behaviours after feedback	6 studies of higher quality; 2 of lower quality	Level 2b
Mini-clinical evaluation exercise			
4 studies, 123 participants	Participants reported they were satisfied with the exercise	All 4 studies of higher quality	Level 1
Direct observation of procedural skills			
1 study, 25 participants	Self report that assessment helped improve clinical skills	Single study of lower quality	Level 2b
Case based discussion			
No studies identified			
Multiple assessment methods			
3 studies, 1051 participants	Mixed reports of satisfaction with assessments	1 study of higher quality, 2 of lower quality	Level 1

*Barr's adaptation of Kirkpatrick's evaluation model. Evaluates outcomes as level 1 (learner's reactions), 2a (modification of attitudes and perceptions), 2b (acquisition of knowledge and skills), 3 (change in behaviour), 4a (change in organisational practice), 4b (benefits to clients or patients).

CME

Follow the link from the online version of this article to obtain certified continuing medical education credits

Effects of glucosamine, chondroitin, or placebo in patients with osteoarthritis of hip or knee: network meta-analysis

Simon Wandel,[1 2] Peter Jüni,[1 2] Britta Tendal,[3] Eveline Nüesch,[1 2] Peter M Villiger,[4] Nicky J Welton,[5] Stephan Reichenbach,[1 4] Sven Trelle[1 2]

[1]Institute of Social and Preventive Medicine, University of Bern, Switzerland
[2]CTU Bern, Bern University Hospital, Switzerland
[3]Nordic Cochrane Centre, Righospitalet, Copenhagen, Denmark
[4]Department of Rheumatology, Clinical Immunology and Allergology, Bern University Hospital, Switzerland
[5]Academic Unit of Primary Health Care, Department of Community Based Medicine, University of Bristol, Bristol, UK

Correspondence to: P Jüni, Institute of Social and Preventive Medicine, University of Bern, Switzerland juni@ispm.unibe.ch

Cite this as: *BMJ* 2010;341:c4675
doi: 10.1136/bmj.c4675

This is a summary of a paper that was published on bmj.com as *BMJ* 2010;341:c4675

STUDY QUESTION

What effect do glucosamine, chondroitin, or the two in combination have on joint pain and on radiological progression of disease in patients with osteoarthritis of the hip or knee?

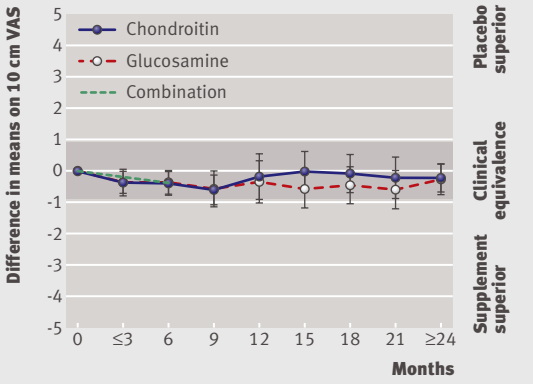
SUMMARY ANSWER

Compared with placebo, glucosamine, chondroitin, or their combination have no clinically relevant effect on joint pain or narrowing of the joint space.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Chondroitin and glucosamine have been recommended in guidelines, prescribed by general practitioners and rheumatologists, and used by patients as over the counter medications to modify the course of osteoarthritis. In our network meta-analysis chondroitin, glucosamine, or their combination had no clinically relevant effect on perceived joint pain or joint space narrowing.

EFFECT OF SUPPLEMENTS ON PAIN IN PATIENTS WITH OSTEOARTHRITIS OVER TIME



Selection criteria for studies

From the Cochrane Controlled Trials Register, Medline, Embase, and CINAHL (from inception to June 2010) we identified randomised trials with an average of at least 100 randomised patients with knee or hip osteoarthritis in each comparison group. Trials compared chondroitin sulfate, glucosamine sulfate, glucosamine hydrochloride, or the combination of any two with placebo or head to head. We excluded doses of chondroitin <800 mg/day or glucosamine <1500 mg/day.

Primary outcome

The main outcome was absolute pain intensity reported in any of nine time windows organised in increments of three months, up to 3, 6, 9, 12, 15, 18, and 21 months and 22 months or more. The secondary outcome was change of minimum radiographic width of joint space between baseline and end of treatment.

Main results and role of chance

We included 10 trials of satisfactory methodological quality with 3803 patients. On a 10 cm visual analogue scale the difference in pain intensity compared with placebo was −0.4 cm for glucosamine (95% credible interval −0.7 to −0.1 cm), −0.3 cm for chondroitin (−0.7 to 0.0 cm), and −0.5 cm for the combination of glucosamine and chondroitin (−0.9 to 0.0 cm). The 95% credible interval did not cross the boundary of the minimal clinically important difference for any of the estimates. Industry independent trials showed smaller effects than commercially funded trials (P=0.02 for interaction). The differences in changes in minimal width of the joint space were all minute, with 95% credible intervals overlapping zero.

Bias, confounding, and other reasons for caution

Network meta-analysis makes similar assumptions to standard meta-analysis of direct comparisons within trials but requires that these assumptions hold over the entire set of trials in the network—that is, for the indirect comparisons also. In addition, our model assumes that relative treatment effects comparing two interventions in different trials are from the same common distribution. Though these assumptions were met, the tests used to evaluate the assumptions have low power.

Study funding/potential competing interests

The study was funded by grants from the Swiss National Science Foundation's National Research Program 53 on musculoskeletal health (PJ and SR) (No 4053-0-104762/3). PJ was a senior research fellow in the Program for Social Medicine, Preventive and Epidemiological Research funded by the Swiss National Science Foundation (grant No 3233-066377). SR was a recipient of a research fellowship funded by the Swiss National Science Foundation (grant No PBBEB-115067). SW was a recipient of an individual fellowship of the Janggen-Poehn-Foundation. The study sponsor had no role in study design, data collection, data synthesis, data interpretation, writing the report, or the decision to submit the manuscript for publication. None of the authors is affiliated with or funded by any manufacturer of any of the agents evaluated in this study.

Response on bmj.com

"What this well conducted meta-analysis does establish is that proponents of glucosamine as a supplement now have to overturn a wealth of negative evidence if it is to be accepted as a useful treatment. There are large studies now. They do not show the results they promised. As the studies get bigger and more rigorous, the putative effect disappears into the noise."

Michael Vagg, consultant in rehabilitation and pain medicine, Barwon Health

To submit a rapid response, go to any article on bmj.com and select "Respond to this article"

The effect of a multifaceted empowerment strategy on decision making about the number of embryos transferred in in vitro fertilisation: randomised controlled trial

Arno van Peperstraten,[1] Willianne Nelen,[1] Richard Grol,[2] Gerhard Zielhuis,[3] Eddy Adang,[3] Peep Stalmeier,[3 4] Rosella Hermens,[2] Jan Kremer[1]

EDITORIAL by Millonson

[1]Department of Obstetrics and Gynaecology, Radboud University Nijmegen Medical Centre, PO Box 9101, 6500 HB Nijmegen, Netherlands
[2]Scientific Institute for Quality of Healthcare, Radboud University Nijmegen Medical Centre
[3]Department of Epidemiology, Biostatistics and HTA, Radboud University Nijmegen Medical Centre
[4]Department of Radiation Oncology, Radboud University Nijmegen Medical Centre
Correspondence to:
A M van Peperstraten
A.vanpeperstraten@obgyn.umcn.nl

Cite this as: *BMJ* 2010;340:c2501
doi: 10.1136/bmj.c2501

This is a summary of a paper that was published on bmj.com as *BMJ* 2010;341:c2501

STUDY QUESTION

What is the effect of a multifaceted empowerment strategy for couples on use of single embryo transfer after in vitro fertilisation (IVF)?

SUMMARY ANSWER

A multifaceted empowerment strategy encouraged couples to choose single embryo transfer in clinical IVF practice. The strategy increased knowledge, had no substantial side effects, reduced costs, and could be an important tool to reduce the twin pregnancy rate. This trial did not, however, demonstrate the anticipated 25% difference in use of single embryo transfer of the power calculation.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Despite initiatives to encourage the use of single embryo transfer, it was used in only 19% of IVF cycles in Europe. Empowerment of couples was effective at encouraging the use of single embryo transfer.

Design

We carried out a randomised controlled trial with allocation through a computer generated randomisation list. The control group received standard IVF care. In addition, the intervention group received a decision aid on the number of embryos transferred, support of an IVF nurse, and, if couples chose single embryo transfer in the first and second cycle and no pregnancy occurred, the offer of reimbursement by way of an extra IVF cycle.

Participants and setting

The trial was carried out in two hospitals licensed to carry out IVF and three associated clinics. The inclusion criteria were couples on the waiting list for a first IVF cycle, with the woman younger than 40.

Primary outcome(s)

Use of single or double embryo transfer in the first and second IVF cycle.

PATIENT CHOICE AND PREGNANCY OUTCOMES AFTER FIRST IN VITRO FERTILISATION (IVF) CYCLE

	No (%)			
First IVF cycle	Decision aid and support group (n=152)	Standard IVF care group (n=156)	% difference (95% CI)	P value
Choosing single embryo transfer	65 (43)	50 (32)	11 (0 to 22)	0.05
Ongoing pregnancy*	48 (32)	59 (38)	6 (−4 to 17)	0.25
Twin pregnancy	6 (4)	10 (6)	2 (−3 to 7)	0.33

*>12 weeks' gestation.

Main results and the role of chance

Overall, 43% (65/152) of couples in the intervention group chose single embryo transfer compared with 32% (50/156) in the control group (difference 11%, 95% confidence interval 0% to 22%; P=0.05). The control group had 11 more ongoing pregnancies than the intervention group (P=0.27) but four more twin pregnancies as well (P=0.32). The proportion of couples in the intervention group who wanted to decide on the number of transferred embryos themselves increased from 77% to 91%, while this percentage remained 73% in the control group (P<0.001). Levels of both experienced knowledge (P=0.001) and actual knowledge (P<0.001) were higher in the intervention group (n=123) than in the control group (n=132). Couples in the intervention group (n=124) reported better informed choice than those in the control group (n=128; P=0.01).

Harms

None.

Bias, confounding, and other reasons for caution

From our initial power calculation we assumed that we would obtain a difference in use of single embryo transfer of 25%. The 11% (95% confidence interval 0% to 22%) difference between the groups remained below this prespecified goal. We carried out multivariable regression analysis to identify confounders for the difference in use of single embryo transfer. The addition of potential confounders did not change the odds ratio for the 11% difference. Owing to the nature of the intervention it was not possible to blind the participants or IVF doctors to the allocation.

Generalisability to other populations

Globally, IVF is done in different contexts (for example, under legislation for number of embryos transferred, with less patient autonomy, or with some or no reimbursement), which can influence the effects of the empowerment strategy. Despite this, in all settings we would expect couples who understand the risks of twin pregnancies to be more inclined to choose single embryo transfer.

Study funding/potential competing interests

This study was funded by the Netherlands Organisation for Health Research and Development (grant No 45-16-105). We have no competing interests.

Trial registration number

ClinicalTrials.gov NCT00315029.

Paracetamol use in early life and asthma: prospective birth cohort study

Adrian J Lowe,[1 2] John B Carlin,[1 2] Catherine M Bennett,[2] Clifford S Hosking,[3] Katrina J Allen,[1] Colin F Robertson,[1] Christine Axelrad,[1] Michael J Abramson,[4] David J Hill,[1] Shyamali C Dharmage[1 2]

[1]Murdoch Childrens Research Institute, Royal Children's Hospital, Parkville, Vic 3052, Australia
[2]Centre for Molecular, Environmental, Genetic and Analytic Epidemiology, School of Population Health, University of Melbourne, Carlton, Vic 3053, Australia
[3]Department of Paediatrics, John Hunter Children's Hospital, New Lambton, Newcastle, NSW 2305, Australia
[4]Department of Epidemiology and Preventive Medicine, Monash University, The Alfred Hospital, Melbourne, Vic 3004, Australia

Correspondence to: A Lowe
lowe.adrian@gmail.com

Cite this as: *BMJ* 2010;341:c4616
doi: 10.1136/bmj.c4616

This is a summary of a paper that was published on bmj.com as *BMJ* 2010;341:c4616

STUDY QUESTION

Does an association exist between use of paracetamol in early life and risk of childhood asthma?

SUMMARY ANSWER

No association existed between frequency of paracetamol use in the first two years of life and risk of subsequent asthma after adjustment for history of early respiratory infections or when paracetamol use was restricted to non-respiratory tract infections.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Use of paracetamol in early life has been implicated as a cause of asthma by cross sectional studies, but the results of previous studies may have been confounded by indication as respiratory infections in early life are commonly treated with paracetamol and a history of respiratory infections is a known risk factor for asthma. No evidence was found of an independent association between paracetamol use and increased risk of childhood asthma or an association with paracetamol use for non-respiratory tract infections.

Participants and setting

We recruited a community based sample of children with a family history of allergic disease before birth between 1990 and 1994 in Melbourne, Australia, and then followed them until they were 6-7 years of age.

Design, size, and duration

The Melbourne Atopy Cohort Study recruited 620 children. Paracetamol use, including the number of days and the indication, was prospectively documented on 18 occasions from birth to 2 years of age (including days and indication for use). Parental report of asthma was assessed at age 6 and 7 years. We made statistical adjustment to determine the effect of paracetamol on risk of asthma, independent of the effect of respiratory tract infections. We also estimated the effect of paracetamol for the least confounded form of paracetamol use—paracetamol given for non-respiratory illnesses (treatment for physical injury and pain)—on subsequent risk of asthma.

Main results and the role of chance

By 12 weeks of age, 51% (295/575) of children had used paracetamol, and this increased to 97% (556/575) by 2 years. At 6 or 7 years, 80% (495) of the original cohort was followed up; 30% (148) had current asthma. Increasing frequency of paracetamol use was crudely associated with increased risk of childhood asthma (odds ratio 1.18, 95% confidence interval 1.00 to 1.39, per doubling of days of use). However, after adjustment for frequency of respiratory infections in early life this association essentially disappeared (adjusted odds ratio 1.08, 0.91 to 1.29). Paracetamol use for non-respiratory causes was not associated with asthma (crude odds ratio 0.95, 0.81 to 1.12).

Bias, confounding, and other reasons for caution

We made adjustments for the major potential confounders of this association, including sex, family history of asthma, presence of older siblings, and frequency of infections in early life. Because of the high rate of exposure to paracetamol, we could not examine the effect of any versus no paracetamol use.

Generalisability to other populations

As this is a cohort at high risk of asthma, care should be taken in generalising these results to the general population, although no apparent reasons exist to believe that the results should be different.

Study funding/potential competing interests

Nestec (a subsidiary of Nestlé Australia) provided funding for the establishment and early follow-up of this cohort, but have played no role in the current analysis or reporting. Unrelated to the current research, SCD has received a research grant from GlaxoSmithKline, and MJA and CR have acted in advisory roles for GlaxoSmithKline, and MJA has received a research grant from Reckitt Benckiser; these companies might have an interest in these results.

ASSOCIATIONS BETWEEN PARACETAMOL INTAKE DURING EARLY LIFE AND RISK OF CHILDHOOD ASTHMA (N=575)

	Unadjusted		Adjusted*	
Indication for paracetamol	Odds ratio (95% CI)	P value	Odds ratio (95% CI)	P value
Any indication	1.18 (1.00 to 1.39)	0.05	1.08 (0.91 to 1.29)	0.39
Non-respiratory indications	0.95 (0.81 to 1.13)	0.58	0.98 (0.83 to 1.17)	0.85

Associations expressed as effect per doubling of number of days of intake (regression on $\log_2$ (days paracetamol+1)).

*Adjusted for infant's sex, parental history of asthma, presence of older siblings at time of birth, and frequency of infections (upper and lower respiratory tract infections, otitis media, and gastrointestinal infections) during first two years of life.

Effectiveness of oseltamivir on disease progression and viral RNA shedding in patients with mild pandemic 2009 influenza A H1N1: opportunistic retrospective study of medical charts in China

Hongjie Yu,[1] Qiaohong Liao,[1] Yuan Yuan,[2] Lei Zhou,[1] Nijuan Xiang,[1] Yang Huai,[1] Xiuhua Guo,[3] Yingdong Zheng,[4] H Rogier van Doorn,[5] Jeremy Farrar,[5] Zhancheng Gao,[2] Zijian Feng,[1] Yu Wang,[6] Weizhong Yang[6]

[1]Office for Disease Control and Emergency Response, Chinese Centre for Disease Control and Prevention, Beijing, China
[2]Department of Respiratory Internal Medicine, Peking University People's Hospital, Peking University Health Science Centre, Beijing
[3]School of Public Health and Family Medicine, Capital Medical University, Beijing
[4]School of Public Health, Peking University Health Science Centre, Beijing
[5]Oxford University Clinical Research Unit, South East Asia Infectious Diseases Clinical Research Network, Hospital for Tropical Diseases, Ho Chi Minh City, Vietnam
[6]Chinese Centre for Disease Control and Prevention, Beijing

Correspondence to: W Yang **yangwz@chinacdc.cn** and H Yu **yuhj@chinacdc.cn**, Chinese Centre for Disease Control and Prevention, 155 Changbai Road, Changping District, Beijing, 102206, People's Republic of China

Cite this as: *BMJ* 2010;341:c4779
doi: 10.1136/bmj.c4779

This is a summary of a paper that was published on bmj.com as *BMJ* 2010;341:c4779

STUDY QUESTION

What are the clinical features of mild infection with pandemic 2009 influenza A(H1N1) virus and what is the effect of oseltamivir on disease progression and viral RNA shedding?

SUMMARY ANSWER

2009 H1N1 infection is usually an uncomplicated, self limiting acute respiratory illness, though the virus might be shed for longer than seasonal influenza virus. Oseltamivir treatment seems to protect against development of radiographic pneumonia and is associated with shorter duration of fever and viral RNA shedding.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS Neuraminidase inhibitors (especially oseltamivir) have been used to treat patients with pandemic 2009 H1N1 infections and, if given within 48 hours of symptom onset, can reduce severity and duration of symptoms and possibly the risk of complications. Patients with mild 2009 H1N1 infection benefit from oseltamivir, in terms of less radiographic pneumonia and shorter duration of fever and viral RNA shedding.

Participants and setting

Patients with 2009 H1N1 infection confirmed by real time reverse transcription polymerase chain reaction were identified through the national surveillance system in China, and those with available data for chart review were enrolled for analysis.

Design, size, and duration

We carried out an opportunistic retrospective review of medical charts of 1291 patients with confirmed 2009 H1N1 from May to July 2009.

MULTIVARIABLE ANALYSES OF RISK FACTORS ASSOCIATED WITH MILD 2009 H1N1 INFECTION

	OR/β (95% CI), P value
Radiographic diagnosis of pneumonia (OR)*	
No oseltamivir treatment	Reference
Oseltamivir started >2 days after symptom onset	0.09 (0.05 to 0.15), <0.001
Oseltamivir started on symptom day 1-2	0.17 (0.10 to 0.29), <0.001
Prolonged duration of fever (β)†	
Oseltamivir started on symptom day 1-2	Reference
Oseltamivir started >2 days after symptom onset	0.15 (0.11 to 0.19), 0.001
No oseltamivir treatment	0.05 (0.001 to 0.10), 0.044
Not presence of radiographic pneumonia	Reference
Presence of radiographic pneumonia	0.07 (0.01 to 0.12), 0.018
Prolonged duration of viral RNA (β)†	
Oseltamivir started on symptom day 1-2	Reference
Oseltamivir started >2 days after symptom onset	0.13 (0.10 to 0.16), 0.001
No oseltamivir treatment	0.04 (0.01 to 0.07), 0.021
Duration (days) of fever after onset of symptoms	0.026 (0.020 to 0.032), 0.001

*Multivariable logistic regression model.
†General linear model. β >0 indicates variable increases risks and β <0 indicates variable reduces risks.

Main results and the role of chance

The median age of patients was 20 years (interquartile range 12-26); over half (54%) were male. The most common symptoms were fever (64%), cough (67%), sore throat (33%), sputum (19%), and rhinorrhoea (18%). Of 920 patients who underwent chest radiography, 110 (12%) had findings consistent with pneumonia. Some 983 (76%) patients were treated with oseltamivir from a median of symptom day 3 (2-4). No patients required admission to an intensive care unit or mechanical ventilation. In most patients (91%) 2009 H1N1 was shed from one day before onset of symptoms to up to eight days after onset, with a median of 5 (3-6) days after onset. Oseltamivir treatment significantly protected against subsequent development of radiographic pneumonia (odds ratio 0.12, 95% confidence interval 0.08 to 0.18), and initiation within two days of symptom onset reduced the duration of fever and viral RNA shedding.

Bias, confounding, and other reasons for caution

For final analysis, we included only 61% (1291/2126) of patients with confirmed infection identified through surveillance during the study period. The study was inevitably retrospective. For timeliness to inform public health policy, we included only 90% of patients discharged during the study period, and we had no information on patients who were still in hospital when the study ended on 31 July. Not all patients underwent radiography, which could have introduced selection bias. We have no information on why nearly a quarter (24%) of patients who were supposed to receive oseltamivir did not.

Generalisability to other populations

Rigorous clinical management in China, including isolation of all patients with confirmed infection, early oseltamivir treatment, and set discharge criteria including an undetectable viral RNA level, provided us with a unique opportunity to study the clinical features, effectiveness of oseltamivir treatment, and the viral RNA shedding pattern of patients with mild 2009 H1N1. Comparisons with similar small observational studies suggest that the findings could also apply to patients with mild 2009 H1N1 infection in other countries.

Study funding/potential competing interests

This study was supported by grants from US National Institutes of Health (Comprehensive International Program for Research on AIDS grant U19 AI51915), the China-US Collaborative Program on Emerging and Re-emerging Infectious Diseases, South East Asia Infectious Disease Clinical Research Network, and Wellcome Trust Major Overseas Programme, Oxford University Clinical Research Unit, Ho Chi Minh City, Vietnam.