# Probable person to person transmission of novel avian influenza A (H7N9) virus in eastern China, 2013: epidemiological investigation

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**bmj.com**
- News: H7N9 avian flu kills seven and infects 23 in China (*BMJ* 2013;346:f2222)
- News: H7N9 virus is more transmissible and harder to detect than H5N1, say experts (*BMJ* 2013;346:f2568)
- News: H7N9 avian flu infects humans for the first time (*BMJ* 2013;346:f2151)

## STUDY QUESTION

Can the novel avian influenza H7N9 virus be transmitted from person to person and is it efficient at doing so?

## SUMMARY ANSWER

In the two patients studied, novel avian influenza H7N9 probably transmitted from one person to another but the transmissibility was limited and non-sustainable.

## WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Animal experiments indicated that the H7N9 virus can transmit itself by droplet under certain conditions. No definite evidence indicates that the novel virus can transmit itself person to person. This is the first report of probable transmissibility of the novel virus from person to person with detailed epidemiological, clinical, and virological data.

### Participants and setting

Two patients with H7N9, 43 close contacts, and relevant live poultry markets and household and surrounding environments.

### Design

Epidemiological investigation.

### Primary outcomes

Clinical data, history of exposure before the onset of illness in the patients, and results of laboratory testing of pathogens and further analysis of sequences and phylogenetic tree to isolated strains.

### Main results and the role of chance

The index patient (the father) became ill five to six days after his last exposure to poultry. The second patient, his 32 year old daughter, who provided unprotected bedside care in the hospital and had direct contact with the father's oral secretions, had no known exposure to poultry. She developed symptoms six days after her last contact with her father. Both patients had confirmed infection with novel avian influenza H7N9 and were admitted to intensive care. Although treated with oseltamivir, mechanical ventilation, immunological therapy, and fluid resuscitation, both died of multi-organ failure. Two strains were isolated successfully from samples from the patients. Genome sequence and phylogenetic tree analyses showed that both viruses were almost genetically identical. We identified 43 close contacts, including 39 healthcare workers of both patients. They were placed under medical observation for seven days. The daughter's husband had mild illness but had negative results for avian H7N9 by real time reverse transcriptase-polymerase chain reaction. The other 42 close contacts did not receive prophylactic antiviral drug after exposure. Paired serum samples (separated by at least three weeks) were collected from close contacts to ascertain potential person to person transmission as well as asymptomatic and subclinical infections. All 43 close contacts tested negative for avian H7N9 specific haemagglutination inhibition antibodies. High titres of antibodies were detected in serum of the two patients.

**bmj.com video:**
The authors describe their findings in a video abstract on bmj.com

### Bias, confounding, and other reasons for caution

As we could not interview the patients because they were critically ill, we cannot rule out the possibility that the daughter acquired her infection from the environment or other sources, though we believe it less likely. As the sensitivity of haemagglutination assay was not satisfied, subclinical or asymptomatic infections could not be excluded among close contacts. Whole sequence alignment showed that the two isolates from patients were not identical, though the slight differences observed between the two strains were reasonably expected.

### Generalisability to other populations

An isolated case of person to person transmission means there is potential for greater human to human transmission.

### Study funding/potential competing interests

Partly supported by the Innovation Platform for Public Health Emergency Preparedness and Response, the Jiangsu Province Key Medical Talent Foundation, the "333" Projects of Jiangsu Province, Jiangsu Province Science and Technology Support Program, and Jiangsu Provincial Project of Preventive Medicine and Wuxi Development Project of Science and Technology Bureau (CSZ00955, CSZ01051).

# Global eradication rates for *Helicobacter pylori* infection: systematic review and meta-analysis of sequential therapy

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- Letter: Should *H pylori* always be eradicated? (*BMJ* 2012;344:e2145)
- Practice: Diagnosis of *Helicobacter pylori* infection (*BMJ* 2012;344:e828)
- Does *Helicobacter pylori* really cause duodenal ulcers? (*BMJ* 2009;339:b2788)

## STUDY QUESTION

What is the efficacy of sequential therapy for eradication of *Helicobacter pylori* infection compared with other treatments?

## SUMMARY ANSWER

The efficacy of sequential therapy is superior to that of seven day triple therapy and similar to regimens of longer duration or including more than two antimicrobial agents.

## WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Triple treatments including a proton pump inhibitor, clarithromycin, and amoxicillin or metronidazole have lost efficacy (now under 80%); sequential therapy represents a new, and potentially more effective, alternative. Results of the meta-analysis show that the overall efficacy of sequential therapy is 84.3% (95% confidence interval 82.1% to 86.4%).

### Selection criteria for studies

Our data sources were Medline, Embase, and the Cochrane controlled trials register up to May 2013 and abstract books from the major European, American, and Asian gastroenterological meetings. We included randomised controlled trials of sequential therapy compared with other treatments in adult patients never treated before for *Helicobacter pylori* infection.

### Primary outcome(s)

The primary outcomes were the relative risk for success of eradicating the infection and the difference in eradication rates among patients assigned to sequential therapy compared with other treatments. We used a random effects model to pool data. We also calculated prediction intervals.

**Comparison of sequential therapy with other *Helicobacter pylori* eradication regimens**

| Comparator regimen | Relative risk (95% CI) | Prediction intervals | $I^2$ (%) |
|---|---|---|---|
| 7 day triple therapy | 1.21 (1.17 to 1.25) | 1.10 to 1.33 | 29.3 |
| 10 day triple therapy | 1.11 (1.04 to 1.19) | 0.89 to 1.39 | 67.2 |
| 14 day triple therapy | 1.00 (0.94 to 1.06) | 0.83 to 1.19 | 54.3 |
| Bismuth containing quadruple therapy | 1.01 (0.95 to 1.06) | 0.89 to 1.14 | 21.1 |
| Non-bismuth quadruple therapy | 0.99 (0.94 to 1.05) | 0.85 to 1.16 | 52.3 |

### Main results and role of chance

We reviewed and analysed 46 randomised controlled trials, in which 5666 patients were randomised to sequential therapy and 7866 to other (established and new) treatments. The overall eradication rate of sequential therapy was 84.3% (95% confidence interval 82.1% to 86.4%). Sequential therapy was superior to seven day triple therapy (relative risk 1.21, 95% confidence interval 1.17 to 1.25; $I^2$=29.3%), marginally superior to 10 day triple therapy (1.11, 1.04 to 1.19; $I^2$= 67.2%), but not superior to 14 day triple therapy (1.00, 0.94 to 1.06; $I^2$=54.3%), bismuth based quadruple therapy (1.01, 0.95 to 1.06; $I^2$=21.1%), or non-bismuth based quadruple therapy (0.99, 0.94 to 1.05; $I^2$=52.3%). The number needed to treat for sequential therapy versus seven day triple therapy was 6 (95% confidence interval 5 to 7). Data on eradication according to pre-treatment antimicrobial susceptibility testing were available in eight studies, and sequential therapy was able to eradicate 72.8% (61.6% to 82.8%) of the strains resistant to clarithromycin.

### Bias, confounding, and other reasons for caution:

Only four trials, which included less than 10% of all patients randomised to sequential therapy, were at low risk of bias; the remaining studies had problems with concealment of allocation and blinding. We found significant heterogeneity, and subgroup analyses failed to identify plausible explanations. The applicability of the results should also be viewed with caution, as information regarding the efficacy of sequential therapy in several Western countries is lacking. Finally, data on the response of treatments according to pre-treatment sensitivity were available in a minority of the randomised controlled trials, not allowing a thorough analysis of the results.

### Study funding/potential competing interests

The study received no funding. CS has received consulting fees for advisory committees or review panels from Pfizer, Janssen-Cilag, and Sidem and for speaking and teaching from AstraZeneca. NV has received consulting fees for speaking and teaching from AstraZeneca, Takeda, Ironwood, and Otsuka and has ownership interest (stock shareholder) in Meridian Diagnostics and Orexo.

bmj.com Respiratory updates from *BMJ* are at bmj.com/specialties/respiratory-medicine

# Improving antibiotic prescribing in acute respiratory tract infections: cluster randomised trial from Norwegian general practice (prescription peer academic detailing (Rx-PAD) study)

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## STUDY QUESTION

Can prescribing of antibiotics for acute respiratory tract infections by general practitioners be improved by group sessions with colleague based academic detailing, including feedback on own prescriptions?

## SUMMARY ANSWER

Significant reductions occurred in overall antibiotic prescribing rates and in the proportion of broad spectrum antibiotics prescribed.

## WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Multifaceted interventions targeting inappropriate antibiotic use may improve general practitioners' prescribing practice. In addition to less frequent antibiotic prescribing for acute respiratory tract infections, the peer academic detailing intervention also led to relatively more use of narrow spectrum antibiotics (penicillin V).

### Design

The randomisation was geographically stratified. The intervention comprised two continuing medical education group meetings with a prescription peer academic detailer (Rx-PAD), focusing on the national guidelines for antibiotic prescribing and recent research evidence. Each general practitioner had to present his or her own prescription report for the others. The control arm received a methodologically similar intervention targeting potentially inappropriate prescriptions for older patients. Both interventions were completed by a regional one day seminar.

### Participants and setting

We invited 250 continuing medical education groups of general practitioners in southern Norway; 80 participated at baseline, and 79 completed the study. We included one year retrospective data from the electronic patient record systems of 440 general practitioners in the continuing medical education groups at baseline, and 382 of them also delivered 12 month post-intervention data.

**Description and changes in rates of antibiotic prescriptions and proportions of non-penicillin V (at CME group level)**

| Outcome | Intervention arm (39 CME groups) | Control arm (40 CME groups) |
|---|---|---|
| Mean (95% CI) proportion (%) of ARTI episodes with antibiotic prescription: | | |
| Before intervention | 31.7 (29.4 to 34.0) | 32.7 (30.2 to 35.2) |
| After intervention | 30.4 (27.9 to 32.8) | 34.2 (31.5 to 37.0) |
| Change | −1.29 (−2.43 to −0.16); −4.1% (relative) | 1.49 (0.58 to 2.40); 4.6% (relative) |
| Mean (95% CI) proportion (%) of penicillin V when antibiotic was prescribed: | | |
| Before intervention | 45.0 (40.8 to 49.2) | 45.2 (40.4 to 50.1) |
| After intervention | 53.8 (49.2 to 58.3) | 43.2 (38.1 to 48.2) |
| Change | 8.74 (5.71 to 11.8); 19.4% (relative) | −2.03 (−3.75 to −0.30); −4.5 % (relative) |

ARTI=acute respiratory tract infection; CME=continuing medical education.

### Primary outcome(s)

The primary outcome was the proportion of acute respiratory tract infection episodes treated with antibiotics and the proportion of prescriptions for narrow spectrum penicillin V in both arms before and after the intervention.

### Main results and the role of chance

For the 39 continuing medical education groups (183 GPs) randomised to this intervention, an adjusted, multilevel model showed that the effect of the intervention was a reduction (odds ratio 0.72, 95% confidence interval 0.61 to 0.84) for prescribing antibiotics for acute respiratory tract infections compared with the control arm of 40 groups (199 general practitioners). Correspondingly, we found a reduction in the odds (0.64, 0.49 to 0.82) for choosing a non-penicillin V antibiotic. The baseline data comprised 124 089 episodes of acute respiratory tract infection, and the post-intervention data comprised 133 258 episodes. In terms of prescriptions per 1000 patients on the general practitioners' lists, the rate increased from 80.3 to 84.6 in the intervention arm and from 80.9 to 89.0 in the control arm, but this reflects a greater incidence of infections (particularly pneumonia) that needed treating in the intervention arm.

### Harms

No harms were reported.

### Bias, confounding, and other reasons for caution

Routine data were collected from everyday practice to reduce bias.

### Generalisability to other populations

The baseline data correspond well with those from all other Norwegian general practitioner specialists, evaluated by proportions of antibiotics typically used for respiratory tract infections. Hence we believe that the results are generalisable to Norwegian general practitioners. Low use of penicillin V in European countries outside Scandinavia makes comparison more difficult.

### Study funding/potential competing interests

The study received grants from the Norwegian Ministry of Health, the Norwegian Medical Association, and the Research Council of Norway. SG has ownership in the company that produced the software for data extraction in this study.

**Trial registration** Clinical trials NCT00272155.

# Effect of telephone health coaching (Birmingham OwnHealth) on hospital use and associated costs: cohort study with matched controls

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**bmj.com/video**
The authors describe the paper's findings in a video abstract

## STUDY QUESTION

What is the effect of routine health coaching via telephone on hospital use and associated costs for patients with long term conditions?

## SUMMARY ANSWER

Telephone health coaching did not lead to the anticipated reductions in hospital admissions or secondary care costs over 12 months, and could have led to increases.

## WHAT IS KNOWN AND WHAT THIS PAPER ADDS

The previous evidence base has been unclear, owing to many studies being small and interventions being heterogeneous. One large randomised controlled trial had found reductions in admissions, but this could have been due to the inclusion of shared decision making for preference sensitive conditions; the present study's findings suggest that interventions could have different effects in routine settings than in trials.

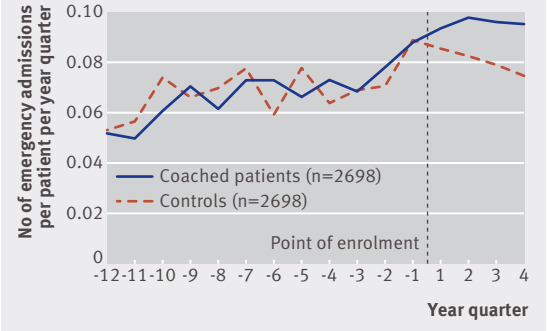
### Participants and setting

Birmingham OwnHealth operated between 2006 and 2012, and recruited patients with long term health conditions from local general practices. Patients receiving health coaching were assigned to care managers, who were specially trained nurses, and received calls that were usually scheduled monthly. The nurses aimed to build continuing relationships with patients and provide motivation, skills, and knowledge to encourage patients to better manage their health conditions (including adherence to treatment, treatment goals, and lifestyle change).

### Design, size, and duration

We studied 2698 patients recruited before 2009 who had a history of hospital use. These individuals were matched on a 1:1 basis to control patients from similar areas of England with respect to demographics, diagnoses of health conditions, previous hospital use, and a predictive risk score. We performed a difference-in-difference analysis against the matched controls to test for effects on urgent and unplanned ("emergency") hospital admissions, elective admissions, outpatient attendances, and notional hospital costs.

**Comparison of rate of emergency admissions**




### Main results and the role of chance

In relation to diagnoses of health conditions and other baseline variables, patients who received health coaching and their matched controls appeared similar before the date of enrolment. Health coaching patients had more emergency admissions in the year after enrolment than in the year before (0.38 *v* 0.31 per head). A smaller increase was observed for matched controls. Overall, the additional increase in hospital admissions associated with the health coaching group was 0.05 per head over 12 months (95% confidence interval 0.00 to 0.09, P=0.046; relative increase 13.6% (0.2% to 27.1%)).

### Bias, confounding, and other reasons for caution

Although the health coaching and matched control groups appeared similar, there may have been unobserved differences, for example, in aspects of disease severity not measured by hospital admissions. We were reassured that both groups had similar levels of in-hospital mortality (2.3% over 12 months) but also simulated the potential effect of unobserved confounding. This showed that, although the increase in emergency admissions could have been caused by unobserved confounding, it is unlikely that we missed a reduction.

### Generalisability to other populations

Unlike many previous randomised controlled trials, we were able to study patients recruited into health coaching in routine settings. However, the effect of health coaching can vary depending on the context in which it is introduced. Design factors that might influence the effect of health coaching include the frequency and content of calls and the extent of care coordination and telemonitoring.

### Study funding/potential competing interests

This study was funded by the Department of Health in England. The health coaching intervention was commissioned by Birmingham East and North Primary Care Trust. AS, IB, and MB have research grants on related topics from funding bodies including the National Institute for Health Research, Technology Strategy Board, and NHS trusts. ST, as an Ernst & Young employee, declares that the consulting firm may undertake consultancy work relevant to the commissioning and provision of community based care. They declare no other competing interests.