RESEARCH

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JACKIE LEWIN/SPL

THIS WEEK'S RESEARCH QUESTIONS

926 Does offering antenatal screening for sickle cell disease and thalassaemia in primary care facilitate earlier uptake of screening?

927 How does high flow oxygen affect mortality in people with acute exacerbation of chronic obstructive pulmonary disease, compared with titrated oxygen?

928 In people receiving opioid substitution treatment, does drug related mortality vary according to duration of treatment?

929 Is China's new cooperative medical insurance scheme for rural citizens associated with changes in operation and use of village health clinics?

High flow oxygen in COPD

Whether or not to give patients with acute exacerbations of chronic obstructive pulmonary disease (COPD) high flow oxygen is controversial. Although some paramedics call concern about this practice "fear mongering" (http://bit.ly/cWTiCn), British Thoracic Society guidelines recommend controlled rather than high flow oxygen in this situation (*Thorax* 2008;63(suppl 6):vi1-68).

Michael Austin and colleagues' study on this approach in 405 patients with presumed acute exacerbation of COPD treated by paramedics in Tasmania, Australia, provides more evidence for the "against" side (p 926). Patients on high flow oxygen had higher mortality than those on titrated oxygen, both overall and in the group with confirmed COPD.

Editorialists B Ronan O'Driscoll and Richard Beasley write that this study "provides robust evidence (p 898); on the other hand, American blogger and retired paramedic Michael Coston points to its shortcomings and suggests it doesn't resolve the issue of which approach to use (http://bit.ly/bt5yHs). He argues: "It is, after all, counterintuitive to deprive someone who is in serious respiratory distress of abundant oxygen." Perhaps this controversy is set to simmer for a while longer.

Antenatal screening for haemoglobinopathies

LIFE IN VIEW/SPL

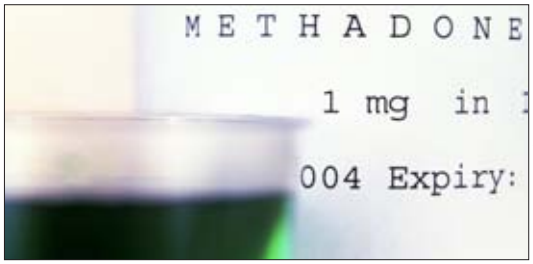
Pregnant women in England should be offered screening for haemoglobinopathies like sickle cell disease and thalassaemia early in gestation so that those with a positive result have the time to make an informed decision about their options, which might include termination. However, only 4.4% of women receive antenatal screening by 10 weeks' gestation, the crucial cut off to enable prenatal diagnostic testing by 13 weeks.

Elizabeth Dormandy and colleagues have found that offering screening when women present to their general practitioner for confirmation of their pregnancy does help improve this rate, but not by much (p 000). Women offered screening by their GP were 17-28% more likely to have been tested by 10 weeks' gestation than women offered screening by a midwife, but the absolute rates of uptake were only 24-28% in the GP groups and 2% in the midwife group.

Writing in an editorial about the research (p 898), general practitioner Judy Shakespeare suggests that by not offering screening early in gestation she and her peers "are failing women with affected pregnancies, who cannot make reproductive choices if professionals 'miss the boat,'" and calls on her colleagues to "take responsibility for testing."

Opioid substitution

Earlier this year we published an observational study (doi:10.1136/bmj.c3172) showing that longer duration of opioid substitution treatment was associated with reduced mortality, but also with a lower likelihood of long term injection cessation. An online rapid response (http://bit.ly/9rjwdh) praised the analysis for "highlighting that opiate addiction is well known to be a chronic disorder, for which most of our information is only short term." The study had limitations, however, including that it was based on data from a single primary care facility in Edinburgh. Now a group including some of the same authors extends its research nationwide in an analysis of data from the UK General Practice Research Database, to investigate changes in risk of death over the duration of substitution treatment. Rosie Cornish and colleagues found that mortality was increased at the start of treatment and immediately after treatment stopped, indicating that a potential reduction in drug related mortality occurs at treatment durations around or above a year (p 928). In an editorial accompanying the earlier paper Evan Wood called for evidence based policy surrounding illicit drugs (doi:10.1136/bmj.c3374). But shortly afterwards, addiction specialists warned that a recommendation from England's National Treatment Agency for Substance Misuse to limit the length of time that methadone can be prescribed in the community was not based on evidence and would do more harm than good (doi:10.1136/bmj.c3998). In this politically controversial field, the more evidence the better. On the practice level, UK doctors who are cautious about recommending substitution treatment may be reassured to hear that the evidence for such therapy holds true in their particular setting.



CORDELIA MOLLOY/SPL

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

Medical care in rural China A podcast at http://podcasts.bmj.com/bmj accompanies the publication of Kimberly Singer Babiarz and colleagues' research on China's New Rural Cooperative Medical Scheme—which aims to provide health insurance to 800 million rural citizens and to correct distortions in rural primary care—and its effect on the operation and use of village health clinics (p 928). We speak to Scott Rozelle from Stanford University and Qingyue Meng, professor and executive director of the China Center for Health Development Studies at Peking University, who explain the background to the formation of the new scheme and its place in the wider Chinese medical system.

Effectiveness of earlier antenatal screening for sickle cell disease and thalassaemia in primary care: cluster randomised trial

SHIFT Study Group

EDITORIAL by Shakespeare

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STUDY QUESTION How effective is offering screening for sickle cell disease and thalassaemia in primary care at facilitating earlier uptake of screening?

SUMMARY ANSWER Offering antenatal screening for sickle cell disease and thalassaemia as part of pregnancy confirmation consultations in primary care increases the proportion of women screened before 10 weeks' gestation.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Antenatal screening for sickle cell and thalassaemia should be offered early in pregnancy but delays are common. This study shows that offering antenatal screening for sickle cell and thalassaemia as part of consultations for pregnancy confirmation in primary care increases the proportion of women screened before 10 weeks' gestation, although only a minority of women were screened before this time, even after intervention.

Design

This was a partial factorial cluster randomised controlled trial. General practices were randomised to three intervention groups for seven months: parallel testing in general practice (tests for sickle cell disease and thalassaemia offered to both parents when pregnancy first reported), sequential testing in general practice (tests offered to mothers when pregnancy first reported, and subsequently to the baby's father if women were found to be carriers), and midwife care (tests offered to mothers at first consultation with a midwife, and subsequently to the baby's father if women were found to be carriers). The study was designed to detect a 20% absolute increase in uptake of screening. The primary outcome was available to all women. Cluster level analyses were adjusted for age group, parity, ethnic group, primary care organisation, and number of general practitioners per practice.

Participants and setting

We recruited women presenting in pregnancy at 25 UK general practices from deprived inner city areas. Data were analysed on 1708 eligible women.

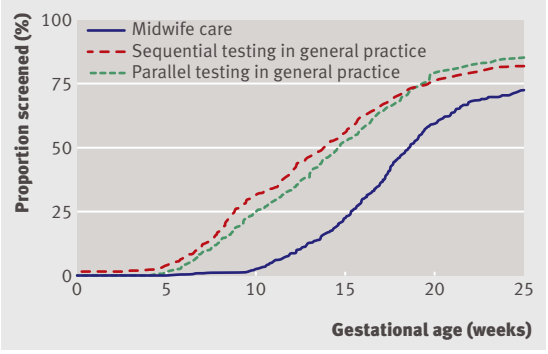
Primary outcome

The primary outcome was the proportion of women screened before 10 weeks' gestation.

Main results and the role of chance

In the midwife care group 2% (9/441) of women were screened by 10 weeks' gestation compared with 24% (161/677) in the GP parallel testing group and 28% (167/590) in the GP sequential testing group. The estimated adjusted difference between midwife care and GP parallel testing groups was 16.5% (95% confidence interval 7.1% to 25.8%; P=0.002) and between midwife care and GP sequential testing groups was 27.8% (14.8% to 40.7%; P<0.001). The proportion of women who knew the carrier status of the baby's father by 11 weeks' gestation was 0% (0/441) in the midwife care group, 2% (13/677) in the GP parallel testing group (P=0.003), and 1% (3/590) in the sequential testing group (P=0.374).

PROPORTION OF WOMEN SCREENED BY GESTATIONAL AGE ACCORDING TO INTERVENTION GROUP



Harms

No adverse events occurred during the trial.

Bias, confounding, and other reasons for caution

Only a minority of eligible practices participated in the trial, and intervention effectiveness may differ when rolled out across all practices. The study was not powered to evaluate effects on reproductive choices and outcomes.

Generalisability to other populations

The study was carried out in an area with a high prevalence of haemoglobin disorders where a universal screening policy was adopted. The results may be less applicable in areas of low prevalence, or in health systems where women present directly to specialists.

Study funding/potential competing interests

This trial was funded by the National Health Status Health Technology Assessment (03/02/03). We have no competing interests.

Trial registration number

The trial is registered as ISRCTN00677850.

Effect of high flow oxygen on mortality in chronic obstructive pulmonary disease patients in prehospital setting: randomised controlled trial

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EDITORIAL by O'Driscoll and Beasley

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STUDY QUESTION In people experiencing breathlessness due to a presumed acute exacerbation of chronic obstructive pulmonary disease in the prehospital setting, does titrated oxygen treatment decrease mortality compared with high flow oxygen treatment?

SUMMARY ANSWER In an intention to treat analysis, mortality was reduced by 58% in the titrated oxygen arm compared with the high flow oxygen arm (relative risk 0.42, 95% confidence interval 0.20 to 0.89; P=0.02).

WHAT IS KNOWN AND WHAT THIS PAPER ADDS Despite audits showing that patients with an exacerbation of chronic obstructive pulmonary disease treated with high flow oxygen have increased mortality, acidosis, and hypercarbia, this treatment remains common. Mortality, acidosis, and hypercarbia were decreased in patients treated with titrated oxygen before admission to hospital, supporting recommendations in the recently published British Thoracic Society guidelines.

Design

This was a cluster randomised, controlled, parallel group trial of titrated oxygen treatment delivered by nasal prongs to achieve arterial oxygen saturations between 88% and 92% compared with high flow oxygen treatment (8-10 l/min). We used computerised random number generation to assign consenting paramedics to treatment groups.

Participants and setting

The study population comprised 405 people aged 35 years or older with breathlessness and a history or risk of chronic obstructive pulmonary disease. Paramedics at the site of the emergency determined the diagnosis on the basis of appropriate acute symptoms, a history of chronic obstructive pulmonary disease (or emphysema) from the patient, or a greater than 10 pack year history of smoking. A diagnosis of chronic obstructive pulmonary disease was confirmed by lung function tests in the previous five years in 214 patients. The participants were transported by ambulance and admitted to the Royal Hobart Hospital, the major general hospital serving southern Tasmania (population approximately 250 000).

EFFECT OF TREATMENT WITH TITRATED OXYGENCOMPARED WITH HIGH FLOW OXYGEN IN ACUTEEXACERBATION OF COPD

Outcome	Treatment effect	P value
Mortality (intention to treat)		
All patients (n=405)	0.42 (0.20 to 0.89)*	0.02
Confirmed COPD (n=214)	0.22 (0.05 to 0.91)*	0.04
Arterial blood gases (<30 min) (confirmed COPD patients; per protocol)		
pH (n=28)	0.12 (0.05)†	0.01
Carbon dioxide (mm Hg) (n=29)	−33.6 (16.3)†	0.02

COPD=chronic obstructive pulmonary disease.
*Relative risk (95% CI).
†Mean difference (SE).

Primary outcome(s)

The primary outcome was prehospital and in-hospital mortality.

Main results and the role of chance

In an intention to treat analysis of all patients, we found a significant difference between the two treatment arms for mortality (relative risk 0.42, 95% confidence interval 0.20 to 0.89; P=0.02). Mortality was 9% (21/226) in the high flow oxygen arm compared with 4% (7/179) in the titrated oxygen arm. Titrated oxygen treatment reduced the risk of death from respiratory failure by 58% for all patients and 78% for patients with confirmed chronic obstructive pulmonary disease, compared with high flow oxygen. For patients with confirmed chronic obstructive pulmonary disease in the prehospital setting, the number need to harm with high flow oxygen was 14.

Harms

No harms were identified.

Bias, confounding, and other reasons for caution

One limitation of the study was the lower than expected rate of adherence to study protocols, in both prehospital oxygen treatment and measurement of arterial blood gases on arrival at hospital. Seventy-nine (37%) participants received treatment that did not comply with the study protocol, although this is likely to have reduced any treatment effect in the intention to treat analysis, and only 19% of arterial samples were taken within 30 minutes of arrival.

Generalisability to other populations

Patients with chronic obstructive pulmonary disease were treated with oxygen in the prehospital setting for an average time of 45 minutes. A dispersed population and lengthy treatment and transport times may maximise the adverse effects of high concentration oxygen treatment compared with areas and services that may have short treatment times.

Study funding/potential competing interests

The Australian College of Ambulance Professionals (ACAP) provided funding. FlaemNova, Milan, Italy, donated Walkie nebulisation air compressors.

Trial registration number

Australian New Zealand Clinical Trials Register ACTRN12609000236291.

Risk of death during and after opiate substitution treatment in primary care: prospective observational study in UK General Practice Research Database

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STUDY QUESTION Does the effect of opiate substitution treatment on drug related mortality vary at the beginning and end of treatment and according to duration of treatment?

SUMMARY ANSWER Mortality was twofold to threefold higher in the first 14 and 28 days of treatment and eightfold to ninefold higher in the month immediately after treatment stopped, compared with the rest of the time on treatment.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS Several studies have shown that the risk of death is reduced during opiate substitution treatment. Mortality is increased at the start of treatment and immediately after treatment stops, which implies that a potential reduction in drug related mortality in the population occurs at average treatment durations approaching or above 12 months.

Participants and setting

We analysed data on patients in the UK General Practice Research Database prescribed methadone or buprenorphine during 1990-2005.

Design, size, and duration

This prospective observational study involved 5577 patients followed-up (17 732 person years) until one year after the expiry of their last prescription for opiate substitution treatment, the date of death before this time had elapsed, or on the date of transfer away from the practice. The main outcome was mortality.

Main results and the role of chance

One hundred and seventy-eight (3%) patients died during follow-up, of whom 62 (35%) died while on treatment. Mortality was almost twice as high among men as in women (mortality rate ratio 2.0, 1.4 to 2.9). The table shows crude and adjusted mortality rates on and off opiate substitution treatment and for the first few weeks on and off treatment. Mortality on and off treatment was 5.3 (95% confidence interval 4.0 to 6.8) and 10.9 (9.0 to 13.1) times higher than the general population. The adjusted death rate in the first month after treatment stopped was more than four times higher (mortality rate ratio 4.20, 2.53 to 6.96) than in the subsequent period off treatment. Our findings suggest that opiate substitution treatment has a greater than 85% chance of reducing overall mortality among opiate users if the average duration approaches or exceeds 12 months.

Bias, confounding, and other reasons for caution

Classification of time on/off treatment was complicated by gaps in prescription information, which may have biased estimates of mortality and diluted or exaggerated the difference between them. Patients who left the database were not actively followed-up, and we had no information on opiate use after patients left treatment; we restricted follow-up to 12 months after treatment, as any misclassification is likely to be small. We had limited covariates for which we could adjust the analyses, and we had no information on quality or intensity of treatment.

Generalisability to other populations

The overall risk of death, standardised mortality ratios, and overall difference in mortality between periods on and off treatment for opiate users in UK primary care are consistent with international literature.

Study funding/potential competing interests

The study was funded by a grant from the National Institute of Health Research (NIHR) for the Centre for Research on Drugs and Health Behaviour. Permission to use the GPRD (protocol 06_058) was funded through the Medical Research Council's licence agreement with the MHRA. At the time they did this work, JM and MH were supported by career scientist fellowship awards from the NIHR. PV is supported by an MRC new investigator award.

CRUDE MORTALITIES AND MORTALITY RATE RATIOS FOR ALL CAUSE MORTALITY ON AND OFF OPIATE REPLACEMENT TREATMENT

				Crude analysis		Adjusted analysis*	
Variable	Deaths	Person years	Mortality/ 100 person years	Mortality rate ratio (95% CI)	P value	Mortality rate ratio (95% CI)	P value
Overall on treatment	62	8939.7	0.69	1.00	<0.001	1.00	<0.001
Overall off treatment	116	8791.8	1.32	1.90 (1.40 to 2.59)		2.29 (1.67 to 3.14)	
Period:							
Weeks 1-2 of treatment	8	471.5	1.70	2.80 (1.33 to 5.91)	<0.001	3.11 (1.47 to 6.59)	<0.001
Weeks 3-4 of treatment	5	378.7	1.32	2.18 (0.87 to 5.47)		2.38 (0.95 to 5.99)	
Remainder of time on	49	8089.4	0.61	1.00		1.00	
Weeks 1-2 off treatment	22	458.0	4.80	7.93 (4.80 to 13.12)		9.01 (5.43 to 14.90)	
Weeks 3-4 off treatment	19	446.6	4.25	7.02 (4.11 to 11.93)		8.01 (4.70 to 13.66)	
Remainder of time off	75	7887.2	0.95	1.57 (1.10 to 2.25)		1.91 (1.32 to 2.76)	

*Adjusted for sex, age group, calendar period, and comorbidity.

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Listen to a podcast with Scott Rozelle and Qingyue Meng, who explain the background to the formation of the New Rural Cooperative Medical Scheme, and its place in the wider Chinese medical system, at www.bmj.com/podcasts

EDITORIAL by Feng

New evidence on the impact of China's New Rural Cooperative Medical Scheme and its implications for rural primary healthcare: multivariate difference-in-difference analysis

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STUDY QUESTIONS Is China's New Rural Cooperative Medical Scheme (NCMS), which aims to provide health insurance to 800 million rural citizens, associated with changes in the operations and use of village health clinics and with the financial risk incurred by individuals?

SUMMARY ANSWER Under NCMS, village clinics experienced increases in weekly patient flow and monthly gross revenue, but no change in annual net revenue, whereas individuals reported a small increase in clinic use and reductions in "out of pocket" medical spending and two measures of exposure to financial risk.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS Previous studies have shown an increase in use of inpatient services at large health centres under NCMS, but findings for outpatient service use and out of pocket spending on healthcare are mixed. This study is the first to use nationally representative data to study the impact of NCMS on village clinics. Results from both provider and household surveys show an increase in clinic use and a drop in the probability of individuals incurring out of pocket expenditures above the 90th percentile of spending among the uninsured and the probability of financing medical care through borrowing or asset sales.

Participants and setting

We collected detailed survey data from 160 village clinics and 8339 individuals in 100 villages spread across five Chinese provinces in 2004 and again in 2007.

Design

We performed difference-in-difference analysis using multivariate linear regressions, controlling for clinic and individual attributes as well as village and year effects, to estimate changes in clinic and individual outcomes.

Primary outcome(s)

Clinic outcomes were log average weekly patient flow, log average monthly gross income, log total annual net income, and the proportion of monthly gross income from medicine sales. Individual outcomes were probability of seeking medical care, log annual "out of pocket" health expenditure, and exposure to financial risk (probability of incurring out of pocket health expenditure above the 90th percentile of spending among the uninsured and probability of financing medical care by borrowing or assets sales).

Main results and the role of chance

Overall, our study found changes among rural village clinics and individuals that are consistent with the objectives of NCMS. Weekly patient flow in village clinics increased by 26%, and the probability that individuals sought medical care from village clinics rose by 5% (with no change in service use from any source). Individual out of pocket medical spending fell by 19% and exposure to the two measures of financial risk declined by 24-63%. These changes also occurred at the county level across the heterogeneous NCMS programmes, even in areas with programmes that had relatively modest benefit packages.

In addition, our findings suggest that the scheme could be placing uncompensated burdens on village clinics. Clinic gross monthly revenue rose by 29%, but net annual revenue did not change. The reduction in service intensity we observed may be desirable, but it appears to be accompanied by responsibilities and costs not reflected on clinic ledgers.

Bias, confounding, and other reasons for caution

An important limitation of our study is the non-random placement of NCMS programmes in villages and the non-random nature of household decisions to participate. Our estimations control for a large number of potentially confounding factors, however, and we have used statistical methods to minimise several sources of likely bias. We also assessed the robustness of our results using other statistical approaches such as propensity score matching.

Generalisability to other populations

Our findings might be generalisable to developing country settings in which policy makers are experimenting with public sector health insurance programmes for poor, rural populations.

Study funding/potential competing interests

The authors received funding from Stanford University's Presidential Fund for Interdisciplinary International Studies, Massachusetts Institute of Technology, the Chinese Academy of Sciences (Science 100 and KSCX2-YW-N-039), and Social Protection in Asia's (SPA) policy research and network building programme. The authors declare no competing interests.

EFFECT OF CHINA'S NEW RURAL COOPERATIVE MEDICAL SCHEME ON VILLAGE CLINIC AND INDIVIDUAL LEVEL OUTCOMES

	Clinic eligibility for scheme reimbursement	Individual participation in the scheme
Village clinic outcomes		
Log average weekly patient flow	0.26* (0.02 to 0.54)	—
Log average monthly gross income	0.29** (0.02 to 0.55)	—
Log total annual net income	0.09 (0.16 to 0.34)	—
Individual outcomes		
Probability of seeking medical care	—	0.01 (0.03 to 0.04)
Log annual out of pocket health expenditure	—	−0.19** (0.36 to 0.02)
Probability of incurring out of pocket health expenditure in the 90th percentile of spending among uninsured	—	0.02* (0.04 to 0.00)

Point estimates for natural log transformed dependent variables can roughly be interpreted as percent changes (or relative changes); estimates from linear probability models can be interpreted as percentage point changes (or absolute changes). Negative point estimates indicate that outcomes have increased less over time in areas with the new rural cooperative medical scheme. 95% confidence intervals reported in parentheses.
Linear probability models include full set of village and year fixed effects, as well as a set of controls for clinic and individual characteristics.
*P<0.10; **P<0.05.