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RESEARCH

THIS WEEK'S RESEARCH QUESTIONS

903 Do testing and treating for chlamydia in sexually active women reduce incidence of subsequent pelvic inflammatory disease?

904 What are the effects of preventive primary care outreach for older adults at risk of functional decline?

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HPV testing on self collected specimens

DELPHI-BIOSCIENCE

Women who do not turn up for cervical screening appointments are at high risk of cervical cancer. Murat Gök and colleagues in the Netherlands investigated sending non-attendees a device to self sample specimens for screening for human papillomavirus, which is found in many cases of cervical cancer (p 905). The proportion of women who received a self sampling kit and submitted a sample was higher than the proportion of women who received a letter re-inviting them to screening and visited their general practitioner for cervical cytology. The cumulative incidence of cervical intraepithelial neoplasia grades II/III or worse in self sampling women was 1.3%, notably higher than the rate of 0.8% found via a regular screening programme in 2005.

Preventive primary care outreach for older people

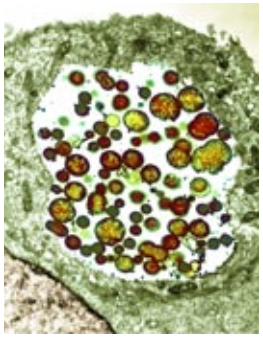
JAMES KING-HOLMES/SPL

One approach to keeping tabs on older people in the community and making sure they're ticking over nicely when they're not acutely unwell is preventive primary care outreach—"proactive, provider initiated care above and beyond demand led routine care." However, Jenny Ploeg and colleagues' study in Canadian adults aged 75 years or older at risk of functional decline found that primary care outreach had no effect on quality adjusted life years, costs of health and social services use, functional status, self rated health, or mortality (p 904).

Domhnall MacAuley, the *BMJ*'s primary care editor, is intrigued as to how a "commonsense" outreach intervention such as the one in this study could have no effect. "Many [outreach specialist services] seem empirically appropriate but don't work," he says.

Chlamydia screening for prevention of PID

Pippa Oakeshott and colleagues' report of the POPI (prevention of pelvic infection) trial was the most read article on bmj.com after its publication last week, and its message seemed to make it out into the wider world too. This randomised trial looked at how effective treatment on the basis of a single positive screening test for chlamydia was at preventing pelvic inflammatory disease (PID) over a year among female students in London (p 903). Compared with delayed treatment, a single episode of screening and treatment made little difference to rates of PID over a year because many screened women were re-infected. The results suggest that the benefits of annual screening might have been overestimated in previous studies and individuals should get re-tested every time they have a new sexual partner.



BIOMEDICAL IMAGING UNIT/SPL

Editorialist Jessica Sheringham fears that the evidence about chlamydia screening's effectiveness is still insufficient to inform policy (p 875). And its cost effectiveness is also uncertain, as highlighted in two recent reports on the United Kingdom's National Chlamydia Screening Programme (launched in 2003 and based on opportunistic testing). The National Audit Office criticised the programme in November 2009 for not testing enough young people, concluding that its delivery "has not demonstrated value for money." In January this year, the Public Accounts Committee confirmed the programme's failure to meet targets and said that the Department of Health "missed an opportunity to refine the programme and to improve its cost effectiveness during the lengthy rollout."

Although the POPI study had limitations—including being underpowered—its findings are important, not least because the opportunity to do a similar trial in England no longer exists. In an online rapid response, Jane S Hocking from the University of Melbourne and her colleagues comment that as screening becomes more ubiquitous, we are running out of chances to do randomised comparisons with unscreened populations (www.bmj.com/cgi/eletters/340/apr08_1/c1642#234418). They say that innovative study designs involving multiple screening rounds and endpoints other than PID are needed to find out whether screening works, and they point to a newly registered cluster randomised controlled trial funded by the Australian government that aims to meet that need (ACTRN12610000297022).

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

Diagnosing serious bacterial infection in young febrile children

Fever is the single most common reason young children present to an emergency department. But how can doctors determine when the febrile illness is caused by a serious bacterial infection such as pneumonia? Jonathan C Craig and colleagues have developed a computerised diagnostic model that uses clinical symptoms and signs to provides an estimate of the risk of serious bacterial infection in children with febrile illness (doi:10.1136/bmj.c1594). When testing the model, the authors found that emergency department physicians tended to underestimate the likelihood of serious bacterial infection in young children with fever, leading to undertreatment with antibiotics.

MARC ROCHE/FOTOLIA

Randomised controlled trial of screening for *Chlamydia trachomatis* to prevent pelvic inflammatory disease: the POPI (prevention of pelvic infection) trial

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EDITORIAL by Sheringham
See also CLINICAL REVIEW, p 912

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"The idea of screening for chlamydia in the general population is practical as women are being screened with the Pap test once in 1-3 years in the reproductive age group. The problem is the lack of it being an effective screening tool and cost effectiveness. Also the number needed to treat would be too high"

Rapid response by Rajasree Pai Ramachandra Pai, resident in internal medicine, University of Connecticut, Storrs, CT, USA

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

STUDY QUESTION Do testing and treating sexually active women for chlamydia reduce the incidence of pelvic inflammatory disease in the subsequent year?

SUMMARY ANSWER Although evidence suggests that screening reduces the incidence of pelvic inflammatory disease, especially in women with chlamydial infection at baseline, the effectiveness of a single chlamydia test in disease prevention over the subsequent year may be overestimated.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS Annual chlamydia testing for sexually active women aged 24 or less is recommended, but the evidence base has been questioned. In our trial, most cases of pelvic inflammatory disease occurred in women without chlamydial infection at baseline, suggesting incident infection which might be reduced by retesting after each new sexual partner.

Design

This was a randomised controlled trial with one year follow-up. Sealed packs containing vaginal swabs were randomly allocated to immediate screening and treatment for chlamydia or deferred screening for a year. Outcomes were assessed blind to group allocation.

Participants and setting

Participants were 2529 sexually active female, multiethnic, London students. Participants completed a questionnaire and provided self taken vaginal swabs. Follow-up was by email, post, or telephone questionnaire, and a search of medical records. As samples might not be tested for a year, the participants were advised to seek testing for chlamydia if they thought they were at risk.

Primary outcome(s)

Incidence of pelvic inflammatory disease over 12 months. Potential cases were identified from questionnaires and records and assessed by three physicians blinded to group allocation and baseline chlamydia status.

Main results and the role of chance

The prevalence of chlamydia at baseline was 5.4% (68/1254) in screened women and 5.9% (75/1265) in controls. Follow-up after 12 months was 94% (2377/2529). Pelvic inflammatory disease occurred in 1.3% (15/1191) and 1.9% (23/1186) of controls (relative risk 0.65, 95% confidence interval 0.34 to 1.22). In women with chlamydial infection at baseline, 9.5% (7/74) of control women (95% confidence interval 4.7% to 18.3%) developed pelvic inflammatory disease over 12 months compared with 1.6% (1/63) of screened women (relative risk 0.17, 0.03 to 1.01). However, most disease (79%, 30/38) occurred in women who tested negative at baseline. Twenty two per cent (527/2377) of participants reported being tested independently during the trial.

Harms

Some women were distressed when told they and their partners needed treatment for chlamydial infection. Although the Aptima (Gen-Probe, San Diego, CA) chlamydia tests used on self taken vaginal swabs have high specificity (98%), false positives are possible.

Bias, confounding, and other reasons for caution

The trial was underpowered because of the lower than expected incidence of pelvic inflammatory disease. We were unable to obtain information on all non-participants, but a survey suggested that women who refused to participate were likely to be from ethnic minority groups. The participants who were tested independently had a high prevalence of chlamydial infection. This probably reduced the effect of the intervention, as did the clinical diagnosis of pelvic inflammatory disease, which lacks sensitivity and specificity. Pelvic inflammatory disease is polymicrobial and only about 30% is due to chlamydia. In addition, 10 women who tested negative for chlamydia at baseline, subsequently tested positive when they were later diagnosed as having pelvic inflammatory disease. Therefore the results were probably diluted by incidental chlamydia infection occurring after the baseline screen, women in the control group being tested later in the year, and pelvic inflammatory disease resulting from causes other than chlamydia.

Generalisability to other populations

Findings may not apply to women attending healthcare facilities; women from different ethnic groups; women not in education; higher risk women, such as sexually active under 16s or sex workers; or non-UK populations.

Study funding/potential competing interests

BUPA Foundation (grant No 684/GB14B). The collecting kits were provided by Gen-Probe (San Diego, CA).

Trial registration number

ClinicalTrials.gov NCT 00115388.

INCIDENCE OF PELVIC INFLAMMATORY DISEASE (PID) IN 2377 SEXUALLY ACTIVE FEMALE STUDENTS FOLLOWED UP OVER 12 MONTHS

	% (No) of women			
Incidence of PID	Screened group	Deferred screening	Relative risk (95% CI)	P value
Overall	1.3 (15/1191)	1.9 (23/1186)	0.65 (0.34 to 1.22)	0.19
Chlamydia positive women at baseline	1.6 (1/63)	9.5 (7/74)	0.17 (0.03 to 1.01)	0.07

Effect of preventive primary care outreach on health related quality of life among older adults at risk of functional decline: randomised controlled trial

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STUDY QUESTION What is the effect of a preventive primary care outreach intervention for older adults at risk of functional decline on quality adjusted life years (QALYs), use and costs of health and social services, functional status, self rated health, and mortality?

SUMMARY ANSWER A preventive primary care outreach intervention for older adults at risk of functional decline had no effect on QALYs, costs of health and social services, functional status, self rated health, or mortality.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS Findings from systematic reviews of preventive interventions for older adults have been inconsistent. Insufficient evidence exists to justify widespread adoption of preventive primary care outreach for this target population of older adults.

Design
This was a randomised single blind trial of older adults allocated into a preventive primary care intervention group or a control group. The 12 month intervention consisted of a comprehensive initial assessment by a home care nurse, collaborative care planning, health promotion, and referral to community health and support services.

Participants and setting
Participants were patients of 35 family physicians in five primary care networks in Hamilton, Ontario, Canada. We included 719 adults aged 75 years and older who were not receiving home care services and who were identified by the Sherbrooke postal questionnaire as being at risk of functional decline.

Primary outcome
The primary outcome measure was quality adjusted life years measured at baseline, six months, and 12 months, with Health Utilities Index Mark 3 health related quality of life utility scores as the quality adjustment weights. Secondary outcome measures included use and costs of health and social services, functional status, self rated health, and mortality.

Main results and the role of chance
The mean difference in QALYs between intervention and control patients was not statistically significant (0.017, 95% confidence interval −0.022 to 0.056; P=0.388). The mean difference in overall cost of prescription drugs and services between the intervention and control groups was not statistically significant (−$C165 (£107; €118; $162), 95% confidence interval −$C16 545 to $C16 214; P=0.984). Changes over 12 months in functional status and self rated health did not differ significantly between the intervention and control groups. Ten patients died in each group. We found no differential effect of the intervention on QALYs for patients at higher or lower risk of functional decline.

Harms
We identified no harms resulting from the intervention.

Bias, confounding, and other reasons for caution
Given that the mortality was lower than expected and the variance inflation on QALYs was larger than expected, we had less power than anticipated to rule out small but potentially important differences in QALYs. Outcome data were collected through reporting by patients.

Generalisability to other populations
We do not know if the 55% of eligible patients who declined to participate were similar to the participants on the variables assessed.

Study funding/potential competing interests
This study was funded by a grant from the Ontario Ministry of Health and Long-Term Care, Primary Health Care Transition Fund. CHG was paid as a consultant to help develop the Health Utilities Index Mark 3 quality of life measure. WF has a stock interest in Health Utilities Inc that distributes copyright Health Utilities Index instrumentation.

Trial registration number Clinical trials NCT00134836.

PATIENTS' OUTCOMES, WITH MULTIPLE IMPUTATION

Outcome	Difference (intervention minus control) (95% CI)	P value
Quality adjusted life years (QALYs)*	0.017 (−0.022 to 0.056)	0.388
Cost of prescription drugs†	−65 (−5849 to 5719)	0.982
Cost of services†	−100 (−14 920 to 14 720)	0.989
Combined costs of prescription drugs and services†	−165 (−16 545 to 16 214)	0.984
Older Americans resources and services multidimensional functional assessment—activities of daily living‡§	0.091 (−0.042 to 0.223)	0.180
Self rated health§¶	−0.015 (−0.158 to 0.127)	0.832

*High score is good (positive difference estimate favours intervention). †$CAN including intervention costs for intervention group (negative difference estimate favours intervention).
‡High score is good (positive difference estimate favours intervention). §12 month value minus baseline value. ¶Low score is good (negative difference estimate favours intervention).

This is a summary of a paper that was published on bmj.com as *BMJ* 2010;340:c1480

HPV testing on self collected cervicovaginal lavage specimens as screening method for women who do not attend cervical screening: cohort study

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STUDY QUESTIONS Does offering self sampling for high risk human papillomavirus (HPV) testing to non-attendees of a cervical screening programme increase the compliance rate, compared with a recall for conventional cytology, and what is the yield of cervical intraepithelial neoplasia (≥CIN II/≥CIN III) in the self sampling group?

SUMMARY ANSWER Offering self sampling by sending a device for collecting cervicovaginal specimens for high risk HPV testing to non-attendees is a feasible and effective method to increase the coverage of screening programmes.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Women not complying with an invitation to the cervical screening programme harbour more than half of the diagnosed cervical carcinomas. The response rate and the yield of high grade lesions both argue for implementation of self sampling for non-attendees of regular screening programmes.

Participants and setting

28 073 women aged 30-60 who were recorded as not attending the regular cervical screening programme in two regions of the Netherlands from December 2006 to December 2007.

Design, size, and duration

Women not responding to two invitations from the programme were randomly assigned (99:1) to receive a device for collecting cervicovaginal material for hybrid capture II high risk HPV testing (n=27 792) or an additional recall for conventional cytology (n=281). Women with a positive test result for high risk HPV on their self sample material were referred to their general practitioner for an additional smear test. Women with abnormal cytology—that is, threshold or borderline/mild dyskaryosis or worse—were referred for colposcopy. Women with normal results on cytology were evaluated after a year by cytology and high risk HPV testing and referred for colposcopy when either of these test results was positive.

Main results and the role of chance

The compliance rate in the self sampling group was notably increased compared with the recall control group (27.5% *v* 16.6%, P<0.001). The self sampling response did not vary with age. Screening history had no influence on participation in self sampling.

The number of detected ≥CIN II and ≥CIN III lesions in self sampling responders was 99/7384 (1.3%) and 76/7384 (1.0%), respectively. Self sampling responders who did not participate in the previous screening round (43%) had increased relative risks of ≥CIN II (relative risk 2.04, 95% confidence interval 1.27 to 3.28) and ≥CIN III (2.28, 1.31 to 3.96) compared with self sampling women who were screened in the round before (57%).

Bias, confounding, and other reasons for caution

We did not use a recall control group to examine the yield of ≥CIN II/≥CIN III compared with the self sampling group because our previous work indicated that non-attendees of the regular screening programme respond poorly to a repeat invitation letter. Therefore we chose 99:1 randomisation to provide sufficient power for detecting the difference in compliance while maximising the yield of ≥CIN II/≥CIN III in the self sampling cohort.

Interestingly, the yields of ≥CIN II and ≥CIN III in the self sampling responders who attended the previous round and the yields in the regular screening responders tested for high risk HPV by general primer 5+/6+ polymerase chain reaction (GP5+/6+ PCR) were identical (0.8% and 0.5%). This strongly suggests that the sensitivity of HPV testing in self sampled material is not inferior to HPV testing on smears taken by a physician.

Generalisability to other populations

Offering self sampling for high risk HPV testing on cervicovaginal material can be used to increase the attendance rate in all countries with an organised screening programme.

Study funding

Delphi Bioscience (formerly Pantarhei Devices), Scherpenzeel, Netherlands, and the screening organisation Noord-Holland and Flevoland, and Comprehensive Cancer Center, Amsterdam. Hybrid Capture-2 kits and UCM were provided by Qiagen, Gaithersburg, MD, USA.

YIELD AND RISK OF ≥CIN III IN WOMEN AGED ≥34 IN RELATION TO PREVIOUS SCREENING

	Screened in previous round		Not screened in previous round			
Age (years)	No of women	≥CIN III	No of women	≥CIN III	Rate of participation in previous round (95% CI)	Relative risk (95% CI) of ≥CIN III
34-38	809	11	688	12*	54.0 (51.5 to 56.6)	1.28 (0.57 to 2.89)
39-43	721	2	545	4*	57.0 (54.2 to 59.7)	2.65 (0.49 to 14.39)
44-48	684	2	455	6*	60.1 (57.2 to 62.9)	4.51 (0.91 to 22.25)
49-53	531	3	387	4*	57.8 (54.7 to 61.0)	1.83 (0.41 to 8.13)
54-58	463	1	362	4	56.1 (52.7 to 59.5)	5.12 (0.57 to 45.57)
≥59	325	—	257	4*	55.8 (51.8 to 59.9)	—
Total	3533	19	2694	34†	56.7 (55.5 to 58.0)	2.28 (1.31 to 3.96)

*Including one carcinoma.
†Including five carcinomas.

The volume-mortality relation for radical cystectomy in England: retrospective analysis of hospital episode statistics

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STUDY QUESTION

Is there a case mix adjusted volume-mortality relation for radical cystectomy in the English healthcare setting?

SUMMARY ANSWER

A volume-mortality relation after radical cystectomy exists at the institution level, and to a lesser degree at the surgeon level. Appropriate interpretation of the relation was, however, only possible after adjustment for institution and surgeon volume effects and structural and process of care confounders.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Centralisation of cancer services has resulted from evidence of a relation between higher volume and better outcomes, but variable results have caused the methodological quality of existing studies to be questioned. At least for radical cystectomy, a relatively infrequent procedure, centralising care to a few institutions should be considered only once the relationship between caseload volume and outcome (including outcomes other than mortality) has been adjusted for structural and process of care confounders such as staffing levels, as well as case mix.

Participants and setting

Patients with a primary diagnosis of cancer undergoing an inpatient elective cystectomy in English hospitals carrying out radical cystectomy in the seven financial years 2000/1 to 2006/7.

Design, size, and duration

A retrospective analysis of hospital episode statistics using multilevel modelling.

Main results and the role of chance

Compared with low volume institutions, medium volume ones had a significantly higher odds of in-hospital and total mortality: odds ratio 1.72 (95% confidence interval 1.00 to 2.98, P=0.05) and 1.82 (1.08 to 3.06, P=0.02). This was seen in the final model only, which included adjustment for structural and process of care factors. There was weak evidence of a reduced odds of in-hospital mortality (by 35%) for high volume surgeons, although this did not reach statistical significance at the 5% level.

Bias, confounding, and other reasons for caution

From the summary of adjusted probabilities figure, medium volume institutions seemed to have worse in-hospital and total mortality than high volume institutions, which is consistent with previous studies. It is unclear why low and high volume institutions seem to have comparable outcomes. Although it would be impossible to refute this finding, it may be artefactual. The division of volumes into thirds does not assume a linear relation between volume and mortality, but rather allows for a non-linear one such as the middle volume having lower or higher mortality than the other two thirds. It is possible that our cut-offs may not be optimal and that more complex functional forms may perform better. The plotting of mortality at unit level against unit volume for our dataset did not reveal any obvious relations. We did not exclude large numbers of very low volume providers, which may have contaminated the low volume third if it contained patient level records present only through coding errors.

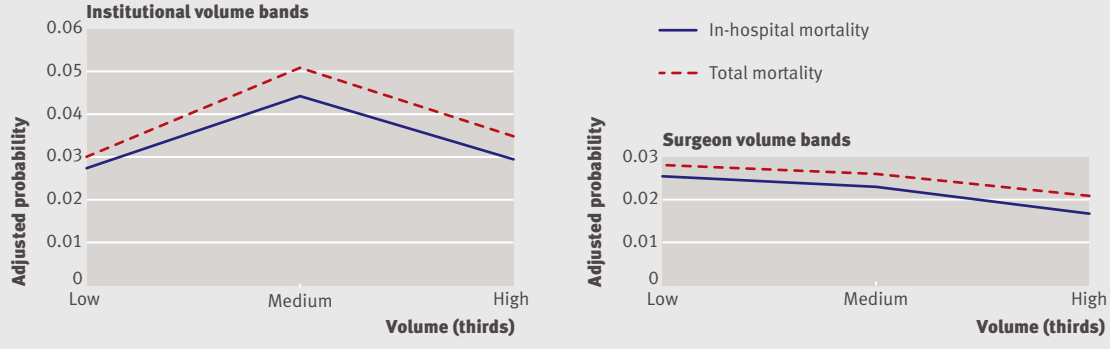
Generalisability to other populations

The use of an incremental modelling approach for volume-outcome research, such as in this study, is in itself important for helping to decide whether volume should be defined at the institution or surgeon level, or both. Using the institution allows for the importance of overall teamwork on outcomes by factoring in institutional factors that cannot always be measured.

Study funding/potential competing interests

AB is based at the Dr Foster Unit, which is funded by a research grant from Dr Foster Intelligence, an independent health service research organisation.

ADJUSTED PROBABILITIES (FROM FINAL MODEL) FOR MORTALITY ACROSS VOLUME BANDS



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