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RESEARCH



THIS WEEK'S RESEARCH QUESTIONS

- 1014** How does human papillomavirus DNA screening with cytology triage compare with conventional cytology for the detection of cervical cancer and severe precancerous lesions?
- 1015** Can a clinical model be developed that estimates more accurately than clinical judgment the likelihood of serious bacterial infection in young children with fever?
- 1016** Is a strategy that uses routine data for risk stratification and then screens people at high risk effective at preventing cardiovascular disease?
- 1017** After a traumatic death, how do bereaved relatives respond to seeing (or being prevented from seeing) the body?

Viewing the body after bereavement by traumatic death

The question of whether it is helpful or hurtful to view the body of a loved one who has died suddenly or traumatically remains controversial and has been tackled by few studies. Chapple and Ziebland's qualitative study (p 1017) aimed to inform the debate, but found no single correct answer. Their interviews with 80 people bereaved through a traumatic death showed a range of good and bad experiences.

The study's findings should, however, be helpful for doctors dealing with this dilemma. The value of viewing the body was affected by whether or not the person thought that they had been given a genuine choice in the matter; those who regretted seeing the body were more likely to have felt "forced" to do so. As Glennys Howarth points out in her editorial (p 988), doctors should make sure that families asked to identify a body understand that they are under no legal obligation, since in this situation the feeling of choice is likely to be lost. Chapple and Ziebland also encourage professionals to pay heed to how a family member refers to the deceased and respect the indication of a continuing social bond if they use the person's name, "him," or "her."

The study's findings lend support to the advice of a recent *BMJ* "Competent Novice" article, in which Paul Frost and colleagues gave junior doctors a step by step breakdown of how to deal with sudden death in hospital (*BMJ* 2010;340:c962). They recommended that families should be given the opportunity to see the body, and they discussed how personal, cultural, and forensic requirements—which may be in conflict with each other—need to be considered during "laying out" and viewing. Chapple and Ziebland's study is the focus of a podcast at podcasts.bmj.com.

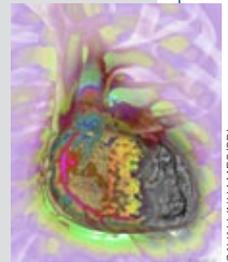


SIMON WINNALL

Stratified screening for cardiovascular disease

In 2008, the Department of Health announced a £250m cardiovascular screening programme for all adults aged 40-74. By undertaking mathematical modelling on data from a well known prospective cohort, EPIC-Norfolk (European Prospective Investigation of Cancer-Norfolk), Parinya Chamnan and colleagues have shown that prestratifying people on the basis of routine data and screening only those at high risk is probably as effective at preventing new cardiovascular events as the universal screening strategy proposed by the government (p 1016).

"These approaches might reduce the economic costs and the potential psychological harm associated with screening tests," say the authors.



CAVALLINI/JAMES/SPL

Identifying serious bacterial infection in children with fever

How can an emergency department doctor determine whether a child presenting with fever has a serious bacterial infection like pneumonia? Jonathan C Craig and colleagues have developed a computerised



CLARE DEPREZ/REPORTERS/SPL

diagnostic model that provides an estimate of the risk of serious bacterial infection in children with febrile illness (p 1015). When testing the model, they found that physicians tended to underestimate the likelihood of serious bacterial infection in young febrile children. The media picked up on this finding, running headlines like "Computers beat doctors at diagnosing child illnesses" (<http://bit.ly/cQrWKO>). However, as editorialists Matthew J Thompson and Ann Van den Bruel point out (p 986), clinicians were as accurate as the model when it came to ruling in serious bacterial infections, they just weren't so good at ruling them out.

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



BUBBLES/PHOTOLIBRARY/ALAMY

Recurrence of severe "morning sickness" across generations

This study found that women whose mothers experienced hyperemesis gravidarum—an extreme form of morning sickness—during pregnancy are three times more likely to experience it themselves than are women whose mothers were not affected (doi:10.1136/bmj.c2050).

Risk of MS in children of sunshine deprived mothers

Low maternal exposure to ultraviolet radiation from sunlight in the first trimester of pregnancy is associated with a raised risk of multiple sclerosis in the infant, according to this Australian study (doi:10.1136/bmj.c1640).

Rate of cervical cancer, severe intraepithelial neoplasia, and adenocarcinoma in situ in primary HPV DNA screening with cytology triage: randomised study within organised screening programme

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STUDY QUESTION Do the rates of detection of cervical cancer and severe precancerous lesions—cervical intraepithelial neoplasia (CIN3+)—differ with primary HPV DNA screening with cytology triage or conventional cytology?

SUMMARY ANSWER Primary HPV DNA screening with cytology triage increases the detection rate of CIN3+ lesions compared with conventional cytology when incorporated into the organised screening programme for cervical cancer.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Screening for HPV could improve detection rates of CIN, but there have been no longitudinal studies on primary HPV DNA screening with cytology triage in routine screening programmes. Compared with conventional screening, primary HPV DNA screening with cytology triage was more sensitive in all age groups' detection of CIN III+. The increase in detection was seen both in the cross sectional findings in women with a positive screening episode and longitudinally in the intensified screening in women initially with borderline findings.

Design

The analysis used an unblinded randomised design integrated within the population based screening programme for cervical cancer. Women were randomly allocated (1:1) to a primary HPV DNA test (hybrid capture II) with cytology triage if the result was positive or to conventional cytological screening (reference).

Participants and setting

The study included 58 076 women aged 30-60 who were invited to a routine population based screening

programme for cervical cancer in southern Finland in 2003-5.

Primary outcomes

Rates of cervical cancer, cervical intraepithelial neoplasia (CIN) grade III, and adenocarcinoma in situ (as a composite outcome referred to as CIN III+), in 2003-7, through a record linkage between the files from screening and cancer registries.

Main results and the role of chance

In the HPV and conventional arms there were 95 600 and 95 700 women years of follow-up, respectively, with 76 and 53 cases of CIN III+ (of which six and eight were cervical cancers). Compared with the conventional arm, the relative rate of CIN III+ in the HPV arm was 1.44 (95% confidence interval 1.01 to 2.05) among all women invited for screening and 1.77 (1.16 to 2.74) among those who actually attended. In women with negative test results, the relative rate of subsequent CIN III+ was 0.28 (0.04 to 1.17).

Harms

In women aged under 35 the rate of positive results was higher in the HPV DNA arm than in the conventional cytology arm. Detection of mild and moderate precancerous lesions (CIN I and II) was higher with HPV DNA screening than with conventional screening.

Bias, confounding, and other reasons for caution

The study was based on individual level randomisation, therefore bias is unlikely to explain the findings, and confounding has been taken care of. Some of the detected cases of CIN III+ could be a result of fluctuations in the diagnostic criteria or health behaviour of screened women.

Generalisability to other populations

Primary HPV DNA screening with cytology triage should be piloted in organised programmes.

Study funding

The study was partially financed by the European Commission through the Europe Against Cancer Action Programme, the Academy of Finland, and the Cancer Organisation of Finland. Funding sources had no involvement in the conduct of the study.

Trial registration number

Current Controlled Trials ISRCTN23885553.

CIN III+ AND RELATIVE RATE (95% CI) BY STUDY ARM FOR ALL WOMEN INVITED FOR CERVICAL SCREENING AND THOSE WHO ATTENDED BY RESULTS OF SCREENING

| | CIN III+ | | RR (95% CI) for comparison between HPV and conventional arms |
|------------------------------------|---------------|------------------------|--|
| | HPV screening | Conventional screening | |
| Invited | 76 | 53 | 1.44 (1.01 to 2.05) |
| Attended | 59 | 33 | 1.77 (1.16 to 2.74) |
| Screening test positive | 57 | 26 | 2.17 (1.38 to 3.51) |
| Screening episode positive | 30 | 16 | 1.86 (1.03 to 3.49) |
| Referred for intensified screening | 27 | 10 | 2.67 (1.34 to 5.80) |
| Screening test negative | 2 | 7 | 0.28 (0.04 to 1.17) |

The accuracy of clinical symptoms and signs for the diagnosis of serious bacterial infection in young febrile children: prospective cohort study of 15 781 febrile illnesses

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EDITORIAL by Thompson and Van den Bruel

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STUDY QUESTION Can a clinical model be developed that estimates more accurately than clinical judgment the probability in children under 5 years with fever?

SUMMARY ANSWER Our computerised diagnostic model that uses routinely collected clinical symptoms and signs can estimate the probability of pneumonia, urinary tract infection, and bacteraemia in children with febrile illness better than clinical judgment alone.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS Clinical scoring systems have been developed to identify serious bacterial infection in children with fever, but few perform well outside of the patient group they were developed in. This study provides a more sophisticated approach to analysing clinical information in order to estimate the probability of the three most common serious bacterial infections in children with a febrile illness. This model could improve clinician decision making by increasing sensitivity for detecting serious bacterial infection, thereby improving use of antibiotics in the acute setting.

Participants and setting

We enrolled children aged less than 5 years of age presenting with a febrile illness to the emergency department of The Children's Hospital at Westmead, Westmead, Australia.

Design, size, and duration

This prospective cohort study initially included 19 889 visits to the emergency department by febrile children between 1

July 2004 to 30 June 2006. A total of 16 742 visits by febrile children were eligible for inclusion. These presentations with fever consisted of 15 781 separate illnesses in 12 807 children. A total of 14 667 illnesses (93%) were followed up until the illness fulfilled the case definition for serious bacterial infection or until the fever had resolved for 24 hours or more.

Main results and the role of chance

The combined prevalence of any of the three infections of interest (urinary tract infection, pneumonia, or bacteraemia) was 7.2% (1140/15 781, 95% confidence interval 6.7% to 7.5%), with urinary tract infection in 543 (3.4%, 3.2% to 3.7%) cases of febrile illness, pneumonia in 533 (3.4%, 3.1% to 3.7%) cases, and bacteraemia in 64 (0.4%, 0.3% to 0.5%) instances.

At the start of this study, an electronic template had been introduced to the record keeping system in the emergency department that standardised the mandatory entry of 40 symptoms and signs for all children presenting with febrile illness. A total of 26 diagnostic variables were selected from the clinical data in the electronic records for inclusion in a multinomial diagnostic model.

The diagnostic model had good test performance for the diagnosis of each type of serious bacterial infection: the area under the receiver operating characteristic curve for urinary tract infection was 0.80 (0.78 to 0.82), for pneumonia was 0.84 (0.83 to 0.86), and for bacteraemia 0.88 (0.84 to 0.92). Early physician estimation of the likelihood of serious infection produced different curves from the probability curves developed by the model, mainly because the majority (85-95%) of physicians estimated that most patients would not have a serious bacterial infection. Thus clinicians mostly underestimated risk of serious bacterial infection and as such did not prescribe antibiotics in 19-34% of cases.

Bias, confounding, and other reasons for caution

Cases of bacteraemia were infrequent (n=64), and as such our model provides a less precise estimation of risk for bacteraemia than for pneumonia and urinary tract infection.

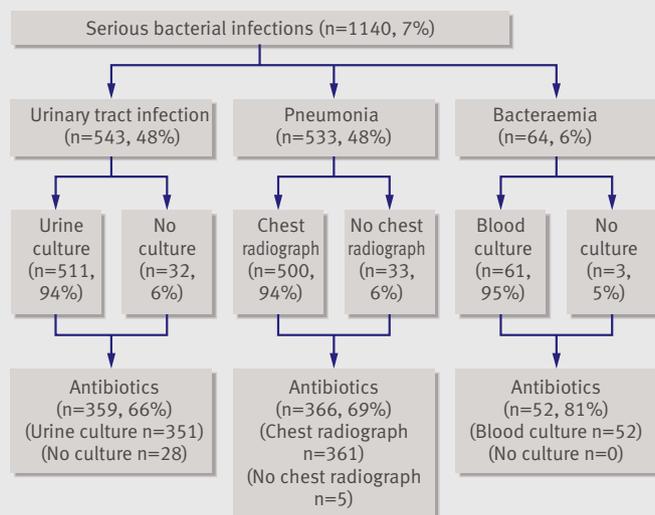
Generalisability to other populations

Children presenting to an emergency department may be more unwell than those attending a primary care facility, hence the incidence of serious bacterial infection and test performance of the clinical algorithm in primary care may differ from those in the current study.

Study funding/potential competing interests

This trial was funded by the National Health and Medical Research Council of Australia. The authors declare no competing interests.

FREQUENCY OF TESTING AND ANTIBIOTIC ADMINISTRATION



Estimating the population impact of screening strategies for identifying and treating people at high risk of cardiovascular disease: modelling study

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EDITORIAL by Marshall

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"Whether there is time to benefit from lifestyle or medical interventions to modify the risk of cardiovascular disease associated with age is not apparent in the results of this study"

Rapid response by Katharine Hartley, specialist registrar in public health, NHS Suffolk
To submit a rapid response, go to any article on bmj.com and click "respond to this article"

STUDY QUESTION Would a strategy using routine data for risk stratification before inviting those at high risk for a cardiovascular risk assessment be as effective at preventing new cardiovascular events as the UK government's recommended mass screening strategy?

SUMMARY ANSWER Inviting people identified at high risk using routine data for a vascular risk assessment could prevent a similar number of new cardiovascular events, with potential cost savings as compared with inviting all adults.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS Despite uncertainty concerning costs and benefits of mass screening, the UK Department of Health recommends that all adults aged 40-74 who have never been identified through self assessment or record based screening, should be invited for cardiovascular risk assessment, which requires people to attend their surgery for biochemical testing. Compared with the government recommended mass screening strategy, an approach using routinely available data for cardiovascular risk stratification before inviting people at high risk for a vascular risk assessment may be similarly effective at preventing new cardiovascular events, with potential cost savings.

Main results

Compared with the government strategy, a stepwise screening approach using a risk score based on routine data could prevent a similar number (lower to upper estimates) of new cardiovascular events annually in the United Kingdom (26 789, 20 778 to 36 239 v 25 134, 19 450 to 34 134) but requiring only 60% of the population to be invited to attend a vascular risk assessment. By inviting all adults aged 50-74 for a vascular assessment, a similar number of cardiovascular events (25 016, 19 563 to 33 372) could also be prevented. Using the

Finnish diabetes risk score questionnaire or anthropometric cut off for risk prestratification was less effective.

Design

Modelling study based on data from 16 970 adults in the EPIC-Norfolk cohort, with assessment of cardiovascular events over 10 years of follow-up.

Source(s) of effectiveness

We examined the potential population impact of different stepwise screening strategies for identifying and treating people at high risk of cardiovascular disease. Relative risk reductions for estimated treatment effects of preventive interventions (smoking cessation, antihypertensive treatment, statin use, and weight management programmes) were derived from meta-analyses of clinical trials or guidelines from the National Institute for Health and Clinical Excellence.

Data sources

Cardiovascular disease outcomes were obtained through linkage records for admission to hospital throughout England and Wales and death certification at the Office for National Statistics. We applied measures of population impact to the UK population estimates for mid-2007.

Results of sensitivity analysis

The main areas of uncertainty were the participation rates following an invitation for vascular risk assessment and the assumption about interactions between multiple preventive interventions. The number of new cardiovascular events that could be prevented increased proportionately with changes in attendance rates. When no additive effect between interventions was assumed, the number of cardiovascular events prevented by each strategy was reduced, but relative comparisons between strategies using routine data and inviting all adults remained unchanged.

Limitations

Using a single point estimate (deterministic approach) for rates of uptake, compliance, and relative risk reduction, without accounting for uncertainty of each estimate, limits insight into the range of these intervention related variables and underestimates the true uncertainty of the population impact.

Study funding/potential competing interests

This study was supported by the Medical Research Council (grant No G950223), Cancer Research UK (grant No C8648A3883), European Union (Europe Against Cancer Programme No 6438). PC is supported by a Royal Thai Government scholarship. SJG receives support from the National Institute for Health Research programme grant funding scheme (RP-PG-0606-1259). We have no competing interests.

POTENTIAL POPULATION IMPACT OF CARDIOVASCULAR DISEASE (CVD) SCREENING STRATEGIES AND PREVENTION INTERVENTIONS IN EPIC-NORFOLK COHORT (N=16 970)

| Strategy | No (%) invited for risk assessment | No needed to attend assessment to prevent one new CVD event | No needed to intervene to prevent one new CVD event | No (lower to upper estimates) of CVD events that could be prevented for UK (26 954 900 adults aged 40-74) |
|--|------------------------------------|---|---|---|
| Strategy 1: age 40-74 | 16 970 (100) | 755 | 107 | 26 789 (20 778 to 36 239) |
| Strategy 2: age ≥ 50 | 12 506 (74) | 596 | 95 | 25 016 (19 563 to 33 372) |
| Strategy 3: body mass index and waist circumference* | 8381 (49) | 527 | 100 | 18 950 (14 332 to 26 555) |
| Strategy 4: FINDRISC ≥ 9 | 6340 (37) | 449 | 96 | 10 087 (7551 to 14 322) |
| Strategy 5: top 60% of Cambridge diabetes risk score | 10 168 (60) | 482 | 91 | 25 134 (19 450 to 34 134) |

FINDRISC=Finnish diabetes risk score.

*Body mass index ≥ 27.5 kg/m², waist circumference > 94 cm in men and > 80 cm in women.

Viewing the body after bereavement due to a traumatic death: qualitative study in the UK

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EDITORIAL by Howarth
PRACTICE, p 1024

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STUDY QUESTION After a traumatic death how do bereaved relatives respond to seeing (or being prevented from seeing) the body?

SUMMARY ANSWER Even after a traumatic and perhaps disfiguring death, relatives need to be given an opportunity to view the body. Social bonds may remain and are indicated when bereaved relatives refer to the body by name or personal pronoun.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS The few studies that have been done suggest that if people choose to see the body they may benefit. This qualitative study includes a wide range of perspectives on viewing the body of a dead friend or relative and helps to explain why the option is important.

Rationale, design, data collection method

Professionals need more evidence to guide them about allowing relatives to view a body after a traumatic and perhaps disfiguring death. Our narrative interview study explored people's experiences of bereavement through traumatic death.

Participants and setting

We interviewed 80 people, in various parts of the UK, bereaved through a traumatic death. Most had seen the body.

Recruitment/sampling strategy

We aimed for a maximum variation sample. People were recruited mainly via support groups, general practitioners, a coroner's officer, a police liaison officer, and a newspaper article.

Data analysis method

A qualitative interpretive approach was taken, combining thematic analysis with constant comparison. We also paid attention to the language that people used during the interviews, particularly how they referred to the body.

Main findings

For those who could choose, decisions about seeing the body varied (including within families). Some wanted someone else to identify the body, because they feared how it might look or preferred to remember their relative as he or she had been in life. Those who had wanted to see the body gave various reasons beyond the need to check identity. Some felt they ought to see the body. Others felt that the body had not lost its social identity, and so wanted to make sure the loved one was "being cared for" or to say goodbye. Some people wanted to touch the body, in private, but the coroner sometimes allowed this only after the postmortem examination, which made relatives feel that the body had become police property. Seeing the body brought home the reality of death;

Examples of people's comments during interviews

Part of Helen's interview—her daughter, Charlotte, died after a drug overdose

- "I sat next to Charlotte for, I don't remember, maybe 15 minutes, and I spoke to her. I think it, it was more important than at the funeral, saying goodbye actually, because she, I could see her"

Part of Rachel's interview—her son died in Iraq when a bomb exploded under his truck

- Interviewer: "Was it the right thing for you to go and see him [in the funeral parlour]?"
- Rachel: "Most definitely, yes, yes, I had to make sure that that was my son, because, you know, they might have made a mistake (...) even though he had lots of injuries and, you know, he had a massive, like, head injury and had snapped his leg, and all down his left side was completely injured, sort of squashed was a better word for it, but it was still him. And even after a week being in Iraq it was still Dave."
- Interviewer: "Mm. So it was the right thing to go and see him?"
- Rachel: "It was definitely the right thing to go and do, yes, definitely."

Part of Sally's interview—her mother died in a fire

- "The worst part, I think, of the whole scenario actually, was actually seeing her. I wish I hadn't done that, that was the worst experience of it actually, and personally I'd never do that, I'd avoid seeing any dead body because I think that was awful."

Extracts from other interviews and analysis are on www.healthtalkonline.org

it could be shocking or distressing, but, in this sample, few who did so said they regretted it.

Implications

Relatives should be given the opportunity to view the body. Officials should prepare them for what they might see. The way that relatives refer to the body can strongly indicate to professionals whether the dead person retains a social identity for the bereaved. We therefore encourage professionals to pay attention to how a family member refers to the body: if they talk about it by name or use a personal pronoun, this should alert clinicians to the continuing sense of social bond and it would be advisable to follow suit rather than speak of the "body," "remains," or "deceased" and risk offence.

Bias, limitations, generalisability

It is quite possible that those who viewed the body may also have been those most likely to take part in an interview for this study. We mainly interviewed white professional people.

Study funding/potential competing interests

The Department of Health funded the work. There are no competing interests.



bmj.com podcasts

Listen to an interview with lead researcher Alison Chapple at <http://podcasts.bmj.com/bmj/>