RESEARCH

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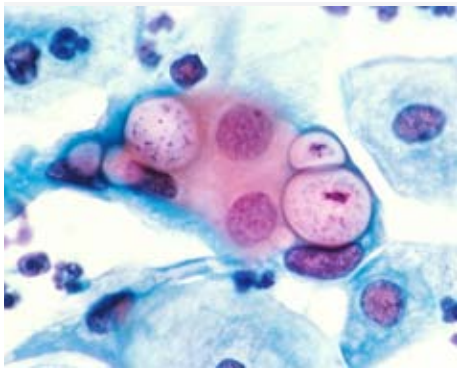

CDC

RESEARCH ONLINE: See www.bmj.com/research

Effect of reducing total fat intake on body weight

According to this meta-analysis of randomised controlled trials and cohort studies, reduction of total fat intake has been achieved in large numbers of both healthy and at risk trial participants over many years. Lower total fat intake leads to small but statistically significant, and clinically meaningful, sustained reductions in body weight in adults in studies with baseline fat intakes of 28-43% of energy intake and durations from six months to over eight years. Evidence supports a similar effect in children and young people, say the authors.

ADAM GAULT/GETTY

WHAT OUR READERS ARE SAYING

Cardiovascular mortality after pre-eclampsia in one child mothers

In this cohort study published on 27 November, excess risk of cardiovascular death was concentrated among women with preterm pre-eclampsia in their first pregnancy and no subsequent children. The association might be due to health problems that discourage or prevent further pregnancies, say the authors, concluding that the risk in women who have term pre-eclampsia in their first pregnancy and go on to have unaffected pregnancies is only modestly raised.

Here's what health economist Oya Eddama concluded in a rapid response:

"The unmeasured variables in this study might be the key to explaining the findings . . . Until we have more of an understanding of the potential causes of pre-eclampsia, including the interplay of lifestyle and social factors, we cannot conclude that pre-eclampsia itself is linked to cardiovascular mortality among these women."

Assessment of best single sample for finding chlamydia in women with and without symptoms: a diagnostic test study

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- Research: Effectiveness of yearly, register based screening for chlamydia in the Netherlands (*BMJ* 2012;345:e4316)
- Research: Costs and cost effectiveness of different strategies for chlamydia screening and partner notification (*BMJ* 2011;342:c7250)

STUDY QUESTION

What is the single best sample for detecting chlamydia in women, with and without symptoms suggestive of an infection?

SUMMARY ANSWER

Self taken vulvovaginal swabs are significantly more sensitive than endocervical swabs for finding chlamydia in women.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

The optimum sample for chlamydia screening in women without symptoms is a self taken vulvovaginal swab. Even in women with symptoms suggestive of an infection, a vulvovaginal swab is superior to endocervical sampling for chlamydia detection. In those women with symptoms, using endocervical rather than vulvovaginal swabs would have missed 9% of infections, or 1 in every 11 cases of chlamydia.

Participants and setting

Participants were women who attended a UK sexual health clinic for testing for sexually transmitted infections.

Design, size, and duration

This study compared diagnostic sample sites. Over 10 months, 3973 women took their own vulvovaginal swab before examination, during which clinicians took an endocervical swab. Samples were analysed by Aptima Combo-2, and positive results were confirmed with the Aptima CT assay, which has a different molecular target. Infected status was defined as a confirmed positive result with either the vulvovaginal or endocervical sample, or both. Samples were processed according to the manufacturer's instructions, and the manufacturer's software determined cut-off values.

Main results and the role of chance

In all, 1671 (42%) of women had symptoms suggestive of a bacterial sexually transmitted infection (vaginal discharge, dysuria, intermenstrual or postcoital bleeding, deep dyspareunia, or lower abdominal pain), and 410 (10.3%) had confirmed infection with chlamydia. Women with chlamydia were significantly more likely to be younger, symptomatic, a contact of a person recently diagnosed with a sexually transmitted infection, and to be diagnosed with cervicitis or pelvic inflammatory disease. Complete sets of paired results were available for 3867 women (106 samples were excluded because of participant errors with the sample tube or staff errors with labelling). Overall sensitivities were 97% for vulvovaginal swabs and 88% for endocervical swabs (P<0.00001). This significant difference is maintained when women with (n=1634) and without (n=2233) symptoms of a bacterial sexually transmitted infection are considered separately. We suggest the difference is due to missed urethral infections when the endocervical site alone is sampled.

The specificity and positive and negative predictive values for the vulvovaginal swabs were 99.9%, 99.5%, and 99.7%, and for the endocervical samples they were 100%, 100%, and 98.7% respectively.

Bias, confounding, and other reasons for caution

This was a single centre study. The order of samples was not randomised. Negative AC2 tests were not confirmed, however, each participant had two different samples analysed for chlamydia so we feel false negatives were correctly identified. As we assessed only one nucleic acid amplification test, the results of this study cannot necessarily be extrapolated to other tests, as their sensitivity and specificity for chlamydia detection can vary.

Generalisability to other populations

This study had a large number of participants examined by 42 different clinicians in a real life clinical situation. The population attending the Centre for Sexual Health at Leeds is similar to many other clinic populations in the UK and other countries, so our findings are widely applicable. Our study supports the continued use of self taken vulvovaginal swabs for chlamydia screening in asymptomatic women. In women with symptoms we recommend either a self taken vulvovaginal swab before examination or a clinician taken vulvovaginal swab before speculum insertion.

Study funding/potential competing interests:

No specific funding, but extra diagnostic reagents and equipment for the study were provided by Gen-Probe (manufacturer of the Aptima Combo-2 assay).

Comparison of vulvovaginal and endocervical swabs for detection of chlamydia infection

	Chlamydia infection status			% Sensitivity (95% CI)	P value*
	Positive	Negative	Total		
Women with symptoms suggestive of bacterial sexually transmitted infection					
Endocervical swab:				88 (83 to 92)	0.0008
Positive	187	0	187		
Negative	26	1421	1447		
Total	213	1421	1634		
Vulvovaginal swab:				97 (93 to 98)	
Positive	206	1	207		
Negative	7	1420	1427		
Total	213	1421	1634		
Women without symptoms suggestive of bacterial sexually transmitted infection					
Endocervical swab:				89 (84 to 93)	0.0025
Positive	163	0	163		
Negative	20	2050	2070		
Total	183	2050	2233		
Vulvovaginal swab:				97 (94 to 99)	
Positive	178	1	179		
Negative	5	2049	2054		
Total	183	2050	2233		

*Endocervical swab compared with vulvovaginal swab.

Assessment of self taken swabs versus clinician taken swab cultures for diagnosing gonorrhoea in women: single centre, diagnostic accuracy study

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STUDY QUESTION

Are self taken vulvovaginal swabs an effective way of diagnosing gonorrhoea?

SUMMARY ANSWER

Self taken vulvovaginal swabs, tested by nucleic acid amplification, are significantly more sensitive at detecting gonorrhoea and have good specificity, compared with culture of urethral and endocervical samples taken by clinicians.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Nucleic acid amplification tests are known to offer increased sensitivity and non-invasive sampling for detecting gonorrhoea, but there are concerns about false positives rates in low prevalence populations. Vulvovaginal swabs tested by the Aptima Combo 2 (AC2) assay had better sensitivity than the culture of urethral and endocervical samples, and had good specificity.

Participants and setting

Women aged 16 years or older and attending an urban sexual health clinic in the United Kingdom, for sexually transmitted infection (STI) testing between March 2009 and January 2010.

Design, size, and duration

This prospective study compared the accuracy of diagnostic tests to detect gonorrhoea. Women took vulvovaginal swabs themselves (for AC2 testing) before examination. During examination, clinicians took urethral and endocervical samples (for culture) and an endocervical swab (for AC2 testing). Culture samples were directly inoculated onto plates and incubated. *Neisseria gonorrhoeae* was confirmed biochemically. Positive samples identified by AC2 were confirmed by Aptima GC, another test with a different molecular target. Gonorrhoea infection was a positive confirmation on either culture or AC2 testing of vulvovaginal or endocervical swabs.

Main results and the role of chance

Of 3973 women, complete sets of results were available for 3859 (114 excluded owing to handling errors). Overall, 100 (2.5%) women had gonorrhoea, of whom 55 were coinfected with chlamydia. Overall sensitivities were 81% for culture, 96% for endocervical swabs using AC2, and 99% for vulvovaginal swabs using AC2. The two AC2 tests were significantly more sensitive than culture (P<0.001). The specificity of culture was acknowledged to be 100%. All positive AC2 results were confirmed by Aptima GC; therefore, specificities and positive predictive values of all tests in all sites were 100%, and negative predictive values of all tests were 99% or greater.

Bias, confounding, and other reasons for caution

This was a single centre study. Despite large numbers of participants, we had no evidence of 3470 (41%) potentially eligible women being offered inclusion into the study. However, each participant acted as her own control, having three different samples analysed for gonorrhoea, thus we believe that the results are valid. The order of samples was not randomised, and our results cannot be extrapolated to other nucleic acid amplification tests, which can have varying sensitivities and specificities.

Generalisability to other populations

This study included a large number of participants examined by 42 different clinicians in a real life clinical setting. The study population attending the Leeds Centre for Sexual Health is comparable with many other clinic populations. We found an overall gonorrhoea prevalence of 2.5% (and 1.9% in women without symptoms suggestive of a bacterial STI) and no false positive results from AC2 tests in this setting. However, in low prevalence settings, even for tests with high specificity, confirmation of a positive result by second test is essential to avoid false positive results.

Study funding/potential competing interests

Gen-Probe provided extra diagnostic reagents and equipment needed for the study. The authors declare no other competing interests.

Trial registration

ISRCTN42867448.

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News: Experts call for more safe sex education as gonorrhoea cases rise by a quarter in England (*BMJ* 2012;344:e3870)

Participants with completed diagnostic tests for gonorrhoea

	Patient infected status (No of women)		Total No of women	Sensitivity (%; 95% CI)	P*
	Positive	Negative			
Gonococcal culture					
Positive	78	0	78	81 (72 to 88)	<0.001
Negative	18	3763	3781		
Total	96	3763	3859		
Clinician taken endocervical swabs and AC2 assay					
Positive	92	0	92	96 (90 to 98)	0.375
Negative	4	3763	3767		
Total	96	3763	3859		
Self taken vulvovaginal swabs and AC2 assay					
Positive	95	0	95	99 (94 to 100)	—
Negative	1	3763	3764		
Total	96	3763	3859		

*Versus self taken vulvovaginal swabs and AC2 assay.

Skin care education and individual counselling versus treatment as usual in healthcare workers with hand eczema: randomised clinical trial

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STUDY QUESTION

Does a secondary intervention programme of skin care education, allergy testing, and individual counselling reduce the severity of hand eczema in healthcare workers?

SUMMARY ANSWER

Healthcare workers self reported statistically significant improvements in hand eczema after the secondary intervention programme.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Primary prevention programmes are known to reduce the development of hand eczema in wet work occupations. Our trial provides evidence that a secondary preventive programme of skin care education and individual counselling based on allergy testing in healthcare workers with mild-moderate hand eczema is associated with improved symptoms, quality of life, self evaluated severity, and protective behaviours.

Design

The trial was a randomised, observer blinded parallel group superiority clinical trial. Randomisation was done centrally and stratified for profession, severity of hand eczema, and hospital. We used a computer generated allocation sequence with a block size of 10. Treatment allocation remained concealed to the clinical investigators. The intervention group received education in skin care and individual counselling based on patch and prick testing and assessment of exposures. The control group received treatment as usual.

Participants and setting

The participants were identified from a survey of 3181 healthcare workers in three Danish hospitals. The inclusion criterion was an affirmative answer to the formerly validated question "Have you had hand eczema during the past 12 months?" 255 of 2269 respondents (11.2%) participated.

Primary outcomes

The primary outcome was clinical severity measured by scores on the hand eczema severity index at five month follow-up. The secondary outcomes were scores on the dermatology life quality index, self evaluated severity, skin protective behaviours, and knowledge of hand eczema from onset to follow-up.

Main results and the role of chance

123 participants were randomised to the intervention and 132 to the control. Follow-up data were available for 247 (97%). At follow-up, the mean score on the hand eczema severity index was significantly lower (improved) in the intervention group than control group (difference of means: unadjusted −3.56 (95% confidence interval −4.92 to −2.14); adjusted −3.47 (−4.80 to −2.14), in both cases P for difference P<0.001), as was the mean score on the dermatology life quality index: difference of means (unadjusted −0.78, non-parametric test P=0.003; adjusted −0.92 (−1.48 to −0.37), P<0.001). Self evaluated severity and skin protective behaviour by hand washings and wearing of protective gloves were also statistically significantly better in the intervention group but this was not the case for knowledge of hand eczema.

Harms: None.

Bias, confounding, and other reasons for caution

As both groups were recruited from the same hospitals we cannot exclude the possibility of contamination of data by spread of information between participants. Individual randomisation was preferred over cluster randomisation to eliminate the risk of differences between the hospitals and to get data from a broader perspective for profession, speciality, and wards. To prevent information bias the participants were individually requested not to share information. Even with the potential risk of contamination, the difference in mean score on the hand eczema severity index between the two groups after five months was statistically significant.

Distributions of primary and two secondary outcome measures in each intervention group

Outcomes	Intervention group	Control group	Difference between means (95% CI)			
			Unadjusted parametric analysis	P for difference	Adjusted parametric analysis	P for difference
Mean (95% CI) HECSI score	4.97 (4.14 to 5.88)	8.53 (7.45 to 9.63)	−3.56 (−4.92 to −2.14)	<0.001	−3.47 (−4.80 to −2.14)	<0.001
Mean (95% CI) DLQI score	1.22 (0.88 to 1.61)	2.00 (1.58 to 2.48)	−0.78, NA	0.003	−0.92 (−1.48 to −0.37)	<0.001
Median (interquartile range) score on knowledge of hand eczema and skin protection	10 (1)	10 (0)	—	0.42	NA	—

HECSI=hand eczema severity index; DLQI=dermatology life quality index; NA=not applicable.
Non-parametric test (Mann Whitney) was used if assumptions of general linear univariate model were not fulfilled.

Comorbidity in patients with branch retinal vein occlusion: case-control study

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STUDY QUESTION

Is branch retinal vein occlusion a consequence of arterial thickening and a marker of arterial rather than venous comorbidities?

SUMMARY ANSWER

Diabetes, hypertension, and peripheral artery disease are associated with an increased risk of incident branch retinal vein occlusion. After a diagnosis of branch retinal vein occlusion, there is an increased risk of developing hypertension, diabetes, congestive heart failure, and cerebrovascular disease. These results are consistent with branch retinal vein occlusion being a consequence of arterial thickening that leads to compression of veins at retinal arteriovenous crossings.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Comorbidity studies have yielded inconsistent results in terms of differentiating between arterial and venous disease, and the role of a disposition towards venous thrombosis is debated. The current large study found an association with arterial disease related to hypertension and supports that investigations and interventions prompted by the diagnosis should focus on arterial hypertension, hyperlipidaemia, and diabetes. Branch retinal vein occlusion in itself does not warrant anticoagulant treatment.

Participants and setting

1168 patients with photographically verified branch retinal vein occlusion and 116 800 control participants alive and aged ≥40 when branch retinal vein occlusion was diagnosed in the corresponding case were included. Data on affected patients were collected between 1976 and 2010 from four secondary referral centres covering about 80% (4.4 million) of the population of Denmark.

Design, size, and duration

In this case-control study with prospective follow-up, we used data from national registries to assess comorbidity within the 10 year period leading up to the diagnosis of branch retinal vein occlusion and a mean of seven years after diagnosis with odds ratios and incidence rate ratios.

Primary outcomes, risks, exposures

Fundus photographs, fluorescein angiograms, and written records from patients examined and registered at the participating institutions were used to identify cases. Hospital discharge diagnoses and dispensing of prescription drugs from national registries were used to assess comorbidities.

Main results and the role of chance

Risk factors present before the diagnosis of branch retinal vein occlusion included peripheral artery disease, diabetes, and arterial hypertension. After diagnosis, patients had an increased risk of developing arterial hypertension (incidence rate ratios, 1.37, 95% confidence interval 1.15 to 1.57), diabetes (1.51, 1.17 to 2.04), congestive heart failure (1.41, 1.12 to 1.68), and cerebrovascular disease (1.49, 1.27 to 1.76), a pattern consistent enough with a predominance of arterial disease rather than venous disease to suggest that the study was well powered to answer the study question.

Bias, confounding, and other reasons for caution

The hospital based diagnoses of branch retinal vein occlusion in this study might have conferred a selection bias in favour of the enrolment of more symptomatic cases, patients most likely to respond to treatment, or fitter patients. These biases could have led to conclusions that differ from population based studies. Diabetic retinopathy makes the diagnosis more challenging, and choosing to exclude patients in whom no clear diagnosis could be made might have biased our study towards identifying a lower impact level for diabetes as a risk factor.

Generalisability

Cases were recruited from Danish outpatient hospital clinics only. Whether the results are generalisable to patients with branch retinal vein occlusion from private practices has not been examined.

Study funding/potential competing interests

The study was funded by the Dag Lenard Foundation.

Logistic regression analyses of risk factors in a one year period before diagnosis of branch retinal vein occlusion

Independent variable	Odds ratio (95% CI)*	P value
Peripheral artery disease	1.83 (1.14 to 2.95)	0.009
Peripheral venous disease	1.96 (0.87 to 4.45)	0.10
Diabetes with end organ damage	2.45 (1.50 to 4.00)	<0.001
Diabetes†	1.74 (1.40 to 2.17)	<0.001
Hypertension†	2.16 (1.86 to 2.51)	<0.001

*Adjusted for age, sex, and year of diagnosis.
†Diagnoses based on both hospital discharge diagnoses and drug prescriptions (remaining diagnoses based on hospital discharge diagnoses only).