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using human papillomavirus testing, and the negative implications for women of missed diagnosis, lifetime colposcopy (64–138%).

We thank those involved in the pilots, including the patients, and the laboratory and primary care staff at the pilot sites who assisted in the collection of workload and cost data; staff at the NHS Purchasing and Supplies Agency for providing indicative market prices of consumables and equipment; and the members of the steering and advisory groups. The views expressed are those of the authors and not necessarily those of the Department of Health.

Contributors: See bmj.com.

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Competing interests: None declared.

Ethical approval: Not required.


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Effects of testing for human papillomavirus as a triage during screening for cervical cancer: observational before and after study

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Abstract

Objective To assess the effect of introducing testing for human papillomavirus combined with liquid based cytology in women with low grade cytological abnormalities.

Design Observational before and after study.


Participants 5654 women aged 20-64 with low grade cytological abnormalities found at routine cervical screening in a pilot; 5254 similar women in the period before the pilot.

Interventions Human papillomavirus testing combined with liquid based cytology in the management of women with borderline or mildly dyskaryotic cervical smear results compared with conventional smear tests, with immediate referral to colposcopy of women positive for human papillomavirus.

Results 57.9% (3187/5506) of women tested in the pilot were positive for human papillomavirus. The rate of repeat smears fell by 74%, but the rate of referral to colposcopy for low grade cytological abnormalities more than doubled. The estimated negative predictive value of human papillomavirus testing varied between 93.8% and 99.7%.

Conclusion The addition of testing for human papillomavirus in women with low grade cytological abnormalities resulted in a reduction in the rate of repeat smears, but an increase in rates of referral to colposcopy.

Members of the pilot studies group are on bmj.com

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Editorial by Schiffman and Castle and p 79

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continued over

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**Introduction**

Oncogenic human papillomavirus has been detected in almost all invasive cancers; its prevalence in precancerous lesions varies from about 80% to 95%. Triaging women with low grade cytological abnormalities on the basis of their human papillomavirus status would reduce requirements for repeat cytology and could improve utilisation of colposcopy; the introduction of liquid based cytology increases the feasibility of DNA testing for human papillomavirus.

**Methods**

The Department of Health commissioned pilot studies in which three cytopathology laboratories in England converted to using liquid based cytology combined with testing for human papillomavirus of women with borderline or mildly dyskaryotic cervical smear results for a 12 month period.

**Results**

A total of 5654 women aged 20-64 in the NHS cervical screening programme had borderline (n = 3797) or mildly dyskaryotic (n = 1857) smear results; 45.6% (1680/3681) and 82.6% (1507/1825) of those women tested, respectively, were positive for human papillomavirus. Respective results by age groups were 64.4% (1239) and 89.0% (1188) for women aged 20-34 years, 29.0% (353) and 69.4% (259) for those aged 35-49 years, and 16.2% (88) and 51.3% (60) for those aged 50-64 years.

Women who tested positive for human papillomavirus were referred for immediate colposcopy. Women who tested negative were referred for colposcopy if at six months cytology showed mild dyskaryosis or worse or they tested positive for human papillomavirus. As the protocol led to increased referral for colposcopy, two centres revised the protocol after six and eight months cytopathology laboratories in England converted to using liquid based cytology combined with testing for human papillomavirus.

For comparison we collected data on 5245 women of a similar age distribution with borderline or mildly dyskaryotic smear results in the 12 months before the pilot, when policy would have been to refer for colposcopy only after, respectively, two or one further abnormal smear results.

Estimated default rates for repeat smears for women negative for human papillomavirus were 19.4% (403/2075) compared with 13.7% for women with low grade abnormalities in the period before the pilot, whereas the estimated default rate for colposcopy in women positive for human papillomavirus and referred directly was 11.2% (264/2358).

In the initial protocol period the rate of repeat smears per woman fell by 70% for borderline smear results from 1.40 to 0.42 (rate ratio 0.30, 95% confidence interval 0.28 to 0.32) and by 87% for mildly dyskaryotic smear results, from 1.18 to 0.15 (0.13, 0.11 to 0.15). The rates of referral for colposcopy for these two categories increased from 15% to 44% (2.92, 2.64 to 3.24) and from 37% to 80% (2.15, 1.93 to 2.40), respectively (table).

**Discussion**

Although rates of repeat smears were reduced after triaging women on the basis of their human papillomavirus status, colposcopy referral rates were increased. Rates of referral to colposcopy after a borderline smear result may have been underestimated for the period before the pilot period. One study reported long term colposcopy and biopsy rates of 42% in a similar group of women. Detection of cervical intraepithelial neoplasia (CIN) grades 2 and 3 increased during the initial protocol period, although this may simply represent more efficient diagnosis of prevalent disease. With the lower screening threshold raised to the age of 25, triage on the basis of human papillomavirus testing for borderline smear results may detect an increased amount of prevalent CIN-2 and CIN-3.

Rates of repeat smears and referral to colposcopy for women with borderline or mildly dyskaryotic smear results according to age group

<table>
<thead>
<tr>
<th>Smear results (age group)</th>
<th>Rate of repeat smears per woman</th>
<th>Rate of referral to colposcopy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before pilot</td>
<td>Pilot</td>
</tr>
<tr>
<td></td>
<td>Initial period</td>
<td>Revised period</td>
</tr>
<tr>
<td>Borderline:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20-34</td>
<td>1.28</td>
<td>0.26</td>
</tr>
<tr>
<td>35-64</td>
<td>1.50</td>
<td>0.61</td>
</tr>
<tr>
<td>Total</td>
<td>1.40</td>
<td>0.42</td>
</tr>
<tr>
<td>Mildly dyskaryotic:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20-34</td>
<td>1.11</td>
<td>0.08</td>
</tr>
<tr>
<td>35-64</td>
<td>1.35</td>
<td>0.35</td>
</tr>
<tr>
<td>Total</td>
<td>1.18</td>
<td>0.15</td>
</tr>
</tbody>
</table>

*For age group 35-64 when protocol remained unchanged.
Risk factors for pulmonary tuberculosis in Russia: case-control study

Richard Coker, Martin McKee, Rifat Atun, Boika Dimitrova, Ekaterina Dodonova, Sergei Kuznetsov, Francis Drobniewski

Abstract

Objectives To determine risk factors for pulmonary tuberculosis in Russia.

Design Case-control study of exposure to a variety of risk factors before and during the development of pulmonary tuberculosis.

Setting Large city in Russia.

Participants Cases were 334 consecutive adults diagnosed as having culture confirmed pulmonary tuberculosis between 1 January 2003 and 31 December 2003. Controls were 334 individuals sampled from a validated population registry, matched for age and sex, and they had no history of tuberculosis. A questionnaire collected information on potential risk factors.

Main outcome measures Risk factors associated with the development of tuberculosis.

Results The main risk factors for tuberculosis were low accumulated wealth (univariate odds ratio 16.70), financial insecurity (5.67), consumption of unpasteurised milk (3.58), diabetes (2.66), living with a relative with tuberculosis (2.94), being unemployed (6.10), living in overcrowded conditions (2.99), illicit drug use (8.74), and a history of incarceration in both pretrial detention centres (5.70) and prison (12.50).

Conclusions When prevalence of exposure is taken into account the most important factors in the development of pulmonary tuberculosis in Russia are exposure to raw milk and unemployment.

Introduction

Rates of tuberculosis in Russia have increased since the break-up of the Soviet Union, but little is known about the risk factors for developing the disease. This case-control study aimed to determine the risk factors for pulmonary tuberculosis in adults in a region of Russia where changes in rates of tuberculosis have mirrored those for the country as a whole.

Methods

We undertook a case-control study in the city of Samara, 700 miles southeast of Moscow. All participants were residents of the city. We defined cases as all adults with culture confirmed pulmonary tuberculosis newly diagnosed at any of the city’s specialist tuberculosis clinics between 1 January 2003 and 31 December 2003, and recruited to a WHO DOTS (directly observed treatment short course) programme. We estimated that 307 cases and an equal number of controls should be recruited to achieve 80% power to detect an odds ratio of 2.0 at the 5% significance level if 10% or more of the general population were exposed to the risk factor. Controls were sampled randomly from the general population of Samara city; they were matched for year of birth and sex, and they had no history of tuberculosis. A team of 22 trained interviewers administered a previously piloted questionnaire to

Contributors: SM led the evaluation team and is the guarantor. AG and RL contributed to the design of the study. HK contributed to the design of the study and chaired the steering group for the pilot studies. Funding: Department of Health Policy Research Programme. Competing interests: None declared. Ethical approval: Not required.


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What is already known on this topic

Testing for human papillomavirus could improve the management of women with borderline or mildly dyskaryotic smear results

Human papillomavirus testing for borderline cytology and colposcopy for women positive for human papillomavirus has greater sensitivity to detect cervical intraepithelial neoplasia grades 2 and 3 than repeat cytology

What this study adds

Triaging women on the basis of testing for human papillomavirus is feasible during cervical screening

Such testing in pilot studies in England led to reduced rates of repeat smears but increased referrals for colposcopy

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