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using human papillomavirus testing, and the negative implications for women of missed disease, lifetime colposcopies (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.

Competing interests: None declared.

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Ethical approval: Not required.


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

Sue Moss, Alastair Gray, Rosa Legood, Martin Vessey, Julietta Patnick, Henry Kitchener on behalf of the Liquid Based Cytology/Human Papillomavirus Cervical Pilot Studies Group

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 Schillman and Castle and p 79

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Rosa Legood senior researcher continued over
Introduction
Oncogenic human papillomavirus has been detected in almost all invasive cancers; its prevalence in precan-
cerous lesions varies from about 80% to 95%. Triageing
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 papilloma-


<table>
<thead>
<tr>
<th>Rate of 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>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.

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. 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 15.7% 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).

Assuming that no high grade disease is present in
those women who remained negative for human papillomavirus at six months (or were not retested) and
were not referred for colposcopy, the negative
predictive value of the human papillomavirus test for
cervical intraepithelial neoplasia grade 2 or worse was
estimated as 99.4% for women with borderline smear
results and 96.5% for those with mildly dyskaryotic
smear results.

This study forms part of the independent evaluation of
the liquid based cytology/human papillomavirus cervical screening
pilot studies commissioned by the Policy Research Programme
at the Department of Health. The evaluation was carried out by
research teams at the Cancer Screening Evaluation Unit,
Institute of Cancer Research (SM, E Henstock), the Health Eco-
nomics Research Centre, University of Oxford (AG, RL), and the
Psychology and Genetics Research Group, King's College Lon-
don (T Marteau, E Mainsi). The views expressed are those of the
authors and not necessarily those of the Department of Health.
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 new patients diagnosed as having culture confirmed pulmonary tuberculosis between 1 January 2003 and 31 December 2003. A questionnaire collected information matched for age and sex to the patients with sample from a validated population registry, 31 December 2003. Controls were 334 individuals diagnosed as having文化 confirmed pulmonary tuberculosis between 1 January 2003 and 31 December 2003, and recruited to a WHO DOTS (directly observed treatment short course) programme.

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Contributors: SM led the evaluation team and is the guarantor. AG and RL participated in the evaluation. MV and JP 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.