Outcome of women with inadequate cervical smears followed up for five years

Y L Hock, S Ramaiah, E S Wall, A M Harris, L Marston, J Marshall, K Kendall, A Teale

Background: The clinical and prognostic significance of “inadequate” cervical smear is unknown, even though women with repeated inadequate smears are referred for colposcopy in the National Health Service (NHS) Cervical Screening Programme.

Aim: To follow up a cohort of women with inadequate cervical smears over the following five years to examine outcomes, including detection of high grade cervical intraepithelial neoplasia (CIN).

Methods: The study comprised 1972 women with an inadequate cervical smear reported at Walsall Hospitals NHS Trust between 1 April 1995 and 31 March 1996. Results of cervical smears and biopsies taken over the following five years were reviewed to confirm the outcome.

Findings: Within five years, 2.2% of women with an inadequate cervical smear developed histologically confirmed high grade CIN, which was higher than the 1.3% seen among all women with cervical smear tests reported at the same laboratory over the same period, although the difference was not significant at the 95% level of confidence. Where inadequacy resulted from or was contributed to by “polymorphs obscuring”, the risk of subsequent development/detection of high grade CIN was 2.6%.

Conclusions: Women with inadequate cervical smears had an increased risk of detection of high grade CIN in the following five years compared with “all women”. This increased risk was not significant, although if a larger number of women had been studied significance may have been reached, so that further studies are needed. The increased risk appeared to be at least partially dependent on the reason for inadequacy.

Methods

The cytology department of Walsall Hospitals NHS Trust serves a population of approximately 253,020 within the Walsall Metropolitan Borough. The laboratory received 25,446 cervical (Papanicolaou) smears between 1 April 1995 and 31 March 1996. These smears were mainly from women of cervical screening age (20–64 years), with a few outliers. All women who had a smear reported as “inadequate” in this period were included in our study group. Inadequate smears were classified according to the reason for inadequacy, using categories recommended by the NHSCSP at the time, as follows:

- Insufficient cellularity (too few squames).
- Poor fixation.
- More than 50% of cellular material obscured by blood, polymorphs, or bacteria (these three groups were considered separately).
- Too thickly spread smear.

Where more than one reason for inadequacy was found the smear was categorised as “multiple reason”.

All these women were followed up for five years. This was so that they had the opportunity of having two negative smears, because we operate three year recall intervals.

Follow up cytology and histology results were retrieved from the laboratory computer system. Where the laboratory computer system did not provide adequate information (that is, patients lost to follow up), the health authority computer system was used to obtain follow up information.

Abbreviations: CIN, cervical intraepithelial neoplasia; NHSCSP, National Health Service Cervical Screening Programme
In accordance with the national guidelines, those with three consecutive inadequate smears, at least two low grade abnormal smears, and one high grade abnormal smear were referred for colposcopy, where biopsies and/or smears were taken.

The subsequent worst abnormality detected was subdivided into three categories, as follows:

1. Smear abnormality only without colposcopic biopsy/histological confirmation.
2. Low grade cervical intraepithelial neoplasia (CIN; colposcopically and histologically confirmed CIN I).
3. High grade CIN (colposcopically and histologically confirmed CIN II, III, or worse).

FINDINGS

Between 1 April 1995 and 31 March 1996, 25 446 cervical smear reports were issued by the laboratory. Of these, 2150 (8.5%) were reported as inadequate, a rate within the national standard range (5–9%). Of the 2150 inadequate reports, 68 were for non-cytological reasons, including request forms received without a smear, or slides that were broken beyond repair being received. Excluding these, 2082 inadequate smears were reported from a total of 25 378 (8.2%). These included a mixture of first, second, and third consecutive inadequate smears, and these related to 1972 women (fig 1).

Table 1 categorises the reasons for inadequacy. In the study population, there were 14 women who had a high grade abnormal smear (moderate dyskaryosis or worse) immediately following an inadequate smear (0.7%). In these cases, all the preceding inadequate smears were reviewed by senior cytology staff, and were confirmed to contain no abnormal (dyskaryotic) cells.

The mean age of women with inadequate smears was 37.7 years, and there were no obvious age differences across the

![Figure 1](http://jcp.bmj.com/)

Outcome of inadequate cervical smears followed up for five years in the 

Walsall district.
Table 2 Subcategorisation within the multiple reasons category, and the subsequent risks of development/detection of high grade CIN, considered in conjunction with related single reason categories

<table>
<thead>
<tr>
<th>Category</th>
<th>Number in category (A)</th>
<th>% Of total inadequate smears (of 1972)</th>
<th>No. of high grade CIN at colposcopy and histology within each category</th>
<th>% Of high grade CIN at colposcopy and histology within each category</th>
<th>No. lost to follow up (B)</th>
<th>No. of inadequates corrected for non-responders (A−B)</th>
<th>Number (%) of high grade CIN at colposcopy and histology within each category corrected for lost to follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple reasons</td>
<td>305</td>
<td>15.47</td>
<td>8</td>
<td>2.62</td>
<td>28</td>
<td>277</td>
<td>8 (2.89%)</td>
</tr>
<tr>
<td>Multiple reasons, including obscured by polymorphs</td>
<td>168</td>
<td>8.52</td>
<td>5</td>
<td>2.98</td>
<td>14</td>
<td>154</td>
<td>5 (3.25%)</td>
</tr>
<tr>
<td>Obscured by polymorphs (single reason)</td>
<td>290</td>
<td>14.71</td>
<td>6</td>
<td>2.07</td>
<td>21</td>
<td>269</td>
<td>6 (2.33%)</td>
</tr>
<tr>
<td>Multiple reasons obscured by polymorphs combined</td>
<td>458</td>
<td>23.23</td>
<td>11</td>
<td>2.40</td>
<td>35</td>
<td>423</td>
<td>11 (2.60%)</td>
</tr>
<tr>
<td>Multiple reasons (including obscured by blood)</td>
<td>105</td>
<td>5.32</td>
<td>1</td>
<td>0.95</td>
<td>10</td>
<td>95</td>
<td>1 (0.50%)</td>
</tr>
<tr>
<td>Obscured by blood (single reason category)</td>
<td>265</td>
<td>13.44</td>
<td>6</td>
<td>2.26</td>
<td>21</td>
<td>244</td>
<td>6 (2.46%)</td>
</tr>
<tr>
<td>Obscured by blood (single reason category) and multiple reasons</td>
<td>370</td>
<td>18.76</td>
<td>7</td>
<td>1.89</td>
<td>31</td>
<td>339</td>
<td>7 (2.06%)</td>
</tr>
<tr>
<td>Obscured by blood – single reason obscured by polymorphs combined</td>
<td>764</td>
<td>38.74</td>
<td>17</td>
<td>2.23</td>
<td>60</td>
<td>704</td>
<td>17 (2.41%)</td>
</tr>
</tbody>
</table>

CIN, cervical intraepithelial neoplasia.
including our own operate three year recall system. Our find-
ings are supportive of current national guidelines requiring
repeated inadequate cervical smears to be referred for colpos-
copy. However, these guidelines do not take into consideration
the reason for inadequacy. Our results suggest that there may
be an association between the reason for inadequacy and the
subsequent risk of detection of high grade CIN. Although the
NHSCSP requires cytology laboratories to report the reason for
inadequacy; this is purely to serve the audit and educational
requirements of the smear takers.

“Our study supports the current guidelines for colpos-
copy in women with repeated inadequate smears by
demonstrating a higher risk of detection of high grade
cervical intraepithelial neoplasia”

Our findings suggest that the increased risk was partially
dependent on the reason for inadequacy. There is no increased
risk of development of high grade CIN if the inadequacy
results from “cytology/obscured by organisms”. However, if
the inadequacy of the smear is caused by other reasons, the
risk of detection of high grade CIN appears to be higher than
that seen in the general population. This risk appears to be
highest when the inadequacy is caused by or contributed to by
“obscured by polymorphs”. A limitation of our study is the
subjective nature of identifying smear adequacy, which may
vary from one screener to another and from one laboratory to
the next. However, a European multicentre study showed a
high level of agreement among cytologists as to what constitu-
ates an inadequate smear.11

Another limitation of our study was the inability to
correlate the clinical signs and symptoms (if there are any)
with colposcopic findings. This is because such findings are
not consistently recorded or are not given to the cytology
laboratory.

Although our study was performed in a single centre, the
findings are probably applicable to other cytology laboratories
in England and Wales. Despite initial optimism that liquid
based cytology would significantly reduce inadequate smear
rates, there is little evidence to support this. There are some
concerns that liquid based cytology might falsely label
inadequate smears as negative, and such an adverse effect
would take several years to become evident in a programme
with a three to five year screening interval.8 Health
technology assessment reports from New Zealand and
Australia also concluded that the introduction of liquid based
cytology was not justified by current evidence.” These
thus, the problem of “inadequate cervical smear” will probably
stay with us for some time, and it is important to understanding
fully its clinical and prognostic significance.

In conclusion, our study supports the current guidelines for
colposcopy in women with repeated inadequate smears by
demonstrating a higher risk of detection of high grade CIN. It
also suggests that colposcopy may not be necessary in a sub-
set of inadequate cervical smears. Because we are required to
practice evidence based medicine, the way forward in our
opinion would be for the NHSCSP to study the outcome (if
possible nationally) of inadequate cervical smears, and to
formulate its guidelines for further management based upon the
evidence.

ACKNOWLEDGEMENTS
We are grateful to Mrs A Turner and Miss S Morris for typing the
manuscript; Ms P Pearmain, Deputy QA Director, West Midlands Cervi-
scinal Screening QA office for her helpful comment on the manuscript;

Take home messages
- Women with inadequate cervical smears had an increased
  risk of detection of high grade cervical intraepithelial neo-
  plasia in the five years following the inadequate smear
  when compared with the total number of women screened
  (2.2% v 1.3%)
- This increased risk was not significant, but if a larger
  number of women had been studied significance may have
  been reached, so that further studies are needed to clarify
  this issue
- The increased risk appeared to be at least partially
  dependent on the reason for inadequacy, with the highest
  risk being seen when inadequacy is caused by or contrib-
uted to by "obscured by polymorphs"

Dr C Livings, Information Manager, West Midlands Cancer Intelli-
gen Unit and C Harris, Medical Student, University of Nottingham
for their statistical advice and analysis; Mrs B Hill for generating rel-
vant data from the computer system; and also Mrs J Brown for
reviewing smears. The study was funded by the West Midlands Cervi-
cal Screening Quality Assurance Reference Centre. It has no involve-
ment in study design, data collection and analysis, in the writing of
the report, or in the decisions to submit the paper for publication.

Authors’ affiliations
Y L Hock, Walsall Hospitals NHS Trust, Manor Hospital, Walsall, West
Midlands WS2 9PS, UK
S Ramaiah, A Teale, Walsall Primary Care Trust, Walsall, West
Midlands WS1 1TE, UK
E S Wall, A M Harris, L Marston, J Marshall, K Kendall, Department of
Cytology, Walsall Hospitals NHS Trust

REFERENCES
2. Department of Health: Department of Health: National Screening
3. Office for National Statistics. Estimates of newly diagnosed cases of
  Statistics. 1998 ONS Monitor MB1 98/2
5. Herbert A. Achievable standards. Benchmarks for reporting and criteria
  for evaluation cervical cytology. Sheffield: NHSCSP, 1995
  and criteria for evaluation cervical cytology. 2nd ed. Sheffield:
7. Sen C, Brett MT. Outcome of women referred to colposcopy for
  referred to colposcopy following inadequate smears. Cytology and
9. Henry JA, Wadebra V. The influence of smear quality on the rate of
detection of significant cervical cytological abnormalities. Acta Cytol
10. Williamson SLM, Hair T, Wadebra V. The effects of different sampling
  techniques on smear quality and the diagnosis of cytological
  abnormalities in cervical screening. Cytology and Pathology 1997;8:188–95.
11. National Institute for Clinical Excellence. Guidance on the use of
  liquid-based cytology for cervical screening. Technology appraisal
12. Herbert A, Johnson T. Personal view. Is it reality or an illusion that
  liquid-based cytology is better than conventional cervical smears?
  in reporting inadequate cervical smears—a multi-centre multinational
14. Broadstock M. New Zealand health technology assessment [NZHTA]
  and semi-automated cervical screening devices. 2000 (available from
  http://nzhta.chmeds.ac.uk)
15. Australian Health Technology Advisory Committee. Review of
  automated and semi-automated cervical screening devices. Canberra:
Outcome of women with inadequate cervical smears followed up for five years

Y L Hock, S Ramaiah, E S Wall, A M Harris, L Marston, J Marshall, K Kendall and A Teale

doi: 10.1136/jcp.56.8.592

Updated information and services can be found at:
http://jcp.bmj.com/content/56/8/592

These include:

**References**
This article cites 7 articles, 0 of which you can access for free at:
http://jcp.bmj.com/content/56/8/592#BIBL

**Email alerting service**
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

**Topic Collections**
Articles on similar topics can be found in the following collections

- Cervical cancer (80)
- Cervical screening (52)
- Gynecological cancer (184)
- Clinical diagnostic tests (805)

**Notes**

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/