### Appendix 5 (as supplied by the authors): Summary of evidence for the effect of screening with cytology on incidence of invasive cervical cancer

<table>
<thead>
<tr>
<th>Quality Assessment</th>
<th>Summary of findings</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cervical cancer</td>
</tr>
<tr>
<td></td>
<td>Screening, no. (%)</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Incidence of invasive cervical cancer</strong></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Randomized trial</td>
</tr>
<tr>
<td>2</td>
<td>Observational study</td>
</tr>
<tr>
<td>13-14†††</td>
<td>Observational studies***</td>
</tr>
</tbody>
</table>

**Note:** CI = confidence interval, HR = hazard ratio, OR = odds ratio, RR = relative risk.

* Random sequence generation unclear and allocation concealment not described; however, study limitations were not downgraded for these risks/uncertainties.
† Inconsistency not applicable for single study.
‡ Directness downgraded owing to concerns regarding population (rural women living in a low-income country) and intervention characteristics (1-time opportunistic screening; short duration [3 mo] of training received by technicians responsible for processing and reading the samples).
§ The number of events is small (<300, a threshold rule of thumb value for dichotomous outcomes); however, considering the specific outcome, the evidence is not downgraded.
¶ Insufficient number of studies to assess publication bias.
** Rates were adjusted for age by study authors.
†† Newcastle-Ottawa Scale for cohort studies was completed; 8 out of a possible 9 stars were awarded.
‡‡ 63 cases of cervical cancer diagnosed in women who had been screened in the 0.5 to 5.5 year interval; 37 of these cases were screen-detected cancers, 26 cases were symptomatic cancers.
§§ 20 cases of cervical cancer diagnosed in women who had been screening in the 0.5 to 5.5 year interval; 6 of these cases were screen-detected cancers, 14 cases were symptomatic cancers.
¶¶ There are 12 included case-control studies†††. The number of studies appears as thirteen because 2 different data sets from 1 study††† were used as separate entries in the meta-analysis.
*** Case-control.
††† Newcastle-Ottawa Scale completed to assess the quality of each of the studies. None of the studies satisfied all of the rating criteria. Despite some uncertainties (e.g., lack of information on non-response rates in some studies) and limitations (e.g., one-third of the studies used hospital controls rather than community controls) the evidence was not downgraded.
††† Heterogeneity statistics were significant: $\chi^2 = 50.98$, 12 degrees of freedom ($p < 0.001$); $I^2 = 76%$. Sensitivity analyses were conducted but heterogeneity could not be explained by differences in study design, populations, interventions, or length of exposure. All studies favour screening; only two of the studies marginally intersect the line of no difference.
§§§ Directness was downgraded due to concerns over the inclusion of both organized and opportunistic screening approaches, the diversity of study locations (both developed and developing...
countries, e.g. Canada, US, Finland, Sweden, Japan, Italy, South Africa, Columbia, Costa Rica, Panama, Mexico), and the related potential for important differences in participants and screening procedures.

Publication bias was strongly suspected owing to asymmetry in the funnel plot and recognition that the risks of publication bias may be substantial for observational studies, particularly small studies that use data from electronic medical records or disease registries.


