Management of women who have had an early sexual debut

For women with a history of sexual abuse or early sexual debut what is the safety and effectiveness of screening using strategies other than those recommended for the general population compared to those recommended for the general population? Recommended population strategy to start screening at 25y. Modified strategy starting <25 years.

Search terms: sexual abuse, adolescent, teenager, child, early sexual debut, early sexual initiation, early sexual intercourse, cervical screening and cervical dysplasia. Articles searched from 2004 to current and limited to the English language.

Results: None of the articles found could directly address the question. A few articles reported age of sexual debut. If provided, usually it is in the form of a range and not directly related to outcomes. Based on feedback from the chair of the Working Party, early sexual debut has been taken as ≤14 years of age. The articles presented below provide findings which may help to evaluate whether women younger than 25 years should be screened for cervical cancer.

Table 1: summary of studies reporting prevalence of cervical abnormalities or invasive cancer in adolescents or association between early sexual debut and cervical cancer

<table>
<thead>
<tr>
<th>Author</th>
<th>Country</th>
<th>Study</th>
<th>Subjects</th>
<th>Findings</th>
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<tbody>
<tr>
<td>Saeed-Vafa et al, 2014</td>
<td>US</td>
<td>Retrospective</td>
<td>92 women 14-20y identified from cytopathology database over 9y period (2001-2009)</td>
<td>Of 8011 women &lt;21y old screened for cervical cancer, 1% (92/8011) had HSIL. Of these 92 women were aged 14-20y, the age at initial cytologic diagnosis of HSIL was 14y for 2 women, 15y for 5 women, 16y for 8 women, 17y for 12 women and 18y for 14 women. Follow-up histology diagnosis was available for 35/92 of which 6 were diagnosed with CIN2+ but ages of cases not provided. Of 8011 no subject developed invasive cervical carcinoma. The author state that delaying cervical screening until 21y is effective for detection of early precancerous lesions.</td>
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<td>Castanon et al, 2013</td>
<td>UK</td>
<td>Audit</td>
<td>1800 women diagnosed with cervical cancer aged 20-29y, from 2007 to 2012 from the National Audit of Invasive Cervical Cancers</td>
<td>Cervical cancer was rare in women aged 20-24 (n=223) compared to women aged 25-29y. 110/223 (49%) cervical cancers were diagnosed at age 24y, 56/223 (25%) at age 23y and 57/223 (26%) at age 20-22y. Cancers in women aged 20-24y tend to be more advanced at diagnosis than those in older women with 20% of women &lt;25y having a stage 2 or worse, vs 6% in women ≥25y (p&lt;0.001). A higher proportion of women 20-24y in comparison with older women were diagnosed with adenosquamous carcinoma and other rarer histological types (10% vs4%, p&lt;0.001).</td>
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Up to age 14y incidence rates of invasive cervical carcinoma were close to zero. Rates increased to 0.15/100,000 females among those 15-19y; rates for this age group have remained unchanged for nearly 40y. On average 14 carcinomas (6 squamous cell, 5 glandular and 3 unspecified) were diagnosed per year among those aged 15-19y (based on 2.7million pap tests or 194,113 pap tests/carcinoma detected).

Table 1: continuation

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<thead>
<tr>
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<tr>
<td>Bernard et al, 2012</td>
<td>US</td>
<td>Longitudinal data analysis</td>
<td>Data from 1999-2008 from 2 federal cancer surveillance programs covering 92% of the US population</td>
<td>The relative risk for invasive cervical carcinoma at age of first intercourse at ≤14 years versus ≥25 years, was 2.05 (95% CI, 1.54-2.73) and for CIN3 it was 2.03 (95% CI, 1.41-2.91) after adjusting for age, study, lifetime number of sexual partners and additional reproductive factors. However, the relative risk for invasive cervical carcinoma in women aged ≤14 years at first intercourse was very similar to that in women aged 16-18 at first intercourse, who likely represent a more relevant comparator in terms of the risk of the Australian female population (median age at first intercourse in Australia is 16-17 years (Rissel et al, 2014; Rissel et al, 2003)).</td>
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<td>International Collaboration of Epidemiological Studies of Cervical Cancer Studies</td>
<td>Multiple</td>
<td>Meta-analysis</td>
<td>Data from 21 studies including 10,773 women with invasive cervical carcinoma, 4,688 CIN3/carcinoma in situ, and 29,164 women without cervical carcinoma.</td>
<td>A pooled analysis of case control studies found that compared to women with an age at 1st sexual intercourse of ≥21y the odds ratio of ICC was 2.31(95%CI 1.85-2.87) for those with an age of 1st sexual intercourse at ≤16y. The increased risk was irrespective of lifetime number of sexual partners. The authors state that the data show a possible additional increase in risk of ICC when the early event of 1st sexual intercourse is shortly followed by a pregnancy.</td>
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<td>Louie et al, 2009</td>
<td>8 developing countries</td>
<td>Pooled IARC case-control studies</td>
<td>1864 invasive cervical carcinomas (ICC) and 1719 controls</td>
<td>Moscicki et al, 2008</td>
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<td>Case et al, 2004</td>
<td>US</td>
<td>Retrospective review</td>
<td>517 women 14-21y with biopsy proven CIN AND follow-up identified from Adolescent referred for colposcopy and biopsy (if lesions were identified) after 3 consecutive cytologies of ASC-US, ASC-US/HPV+ve, LSIL, HSIL or AGC. Median age of sexual activity was 15y and median age of cohort was 17y.</td>
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colposcopy database from 1992-2004

19y. The rate of CIN2/3 in patients with persistent ASCUS, LSIL and HSIL was 35%, 36% and 50%, respectively. No cases of invasive cancer were identified.

**Abbreviations:** AIS: adenocarcinoma in situ; ASC-US: atypical squamous cells of undetermined significance; AGC: atypical glandular cells; CIN: cervical intraepithelial neoplasia, HSIL: high grade squamous intraepithelial lesions; LEEP: loop electrosurgical excisional procedure; LSIL: low-grade squamous intraepithelial lesions; ICC: invasive cervical carcinoma; y: years

**Table 2:** summary of studies reporting the natural history of cervical lesions in adolescents with abnormalities

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<tr>
<td>Wilkinson et al, 2015</td>
<td>New Zealand</td>
<td>Retrospective cohort</td>
<td>123 women &lt;20y and 539 women ≥20y with a diagnosis of CIN1 or CIN2 (total n=662)</td>
<td>Women identified from database of 2 colposcopy units and follow-up data identified to determine recurrence of HG lesions. In the &lt;20y group, 32 cases (31%) of CIN2 spontaneously regressed, 45 cases of CIN2 were treated and 46 cases of CIN1 were conservatively managed. After 2y, there was no significant difference in the risk of development of HG abnormalities between the CIN1 group and the group of women with CIN2 which spontaneously regressed.</td>
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<td>Moscicki et al, 2010</td>
<td>US</td>
<td>Prospective study</td>
<td>95 women aged 13-24y with histologically confirmed CIN2</td>
<td>Women were followed up at 4 month intervals. 38% cleared by 1 year, 63% by year 2 and 68% by year 3. 15% of women progressed by year 3. HPV16/18 persistence and status at last visit was associated with progression. The authors state that the high regression rate of CIN2 support clinical observation in young women.</td>
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<td>Monteiro et al, 2010</td>
<td>Brazil</td>
<td>Cohort study, partly retrospective and partly prospective</td>
<td>147 sexually active females 11-19 years old with cervical intraepithelial lesions</td>
<td>Group split in 2, women who had biopsy and those who did not. Follow-up every 6m. New smears taken at 12 and 24m after diagnosis of CIN lesions. Median time from sexual debut to atypical cytology was 12m and 8.2% had a diagnosis of HSIL from their 1st smear. After 2y of FU, regression was observed in 91% of women with ASCUS cytology, 64% of women with LSIL cytology and 50% of women with HSIL cytology. In the biopsy group, 59.4% of women with CIN1 and 71.4% with CIN2 progressed while 3.1% progressed from CIN1 to CIN2/3.</td>
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<td>Fuchs et al, 2007</td>
<td>US</td>
<td>Retrospective cohort</td>
<td>93 women ≤21y of which 12 were &lt;16, 38 were 17-19y and 43 were 20-21y with biopsy confirmed CIN2, identified from colposc</td>
<td>S/12 women aged ≤16y were referred to colposcopy for HSIL, S/12 for LSIL and 2 for ASC-US. Colposcopy confirmed CIN2 lesions in 7 cases and CIN1/2 lesions in 5 cases. No CIN3 or invasive carcinoma cases were found. 6 women decided on treatment and 6 women had conservative management with 4-6m follow-up. Compared to the other age groups, women ≤16y experienced disease regression at a faster rate. Within 2</td>
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<tr>
<td>Study Authors, Year</td>
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<td>Age Range</td>
<td>Eligibility Criteria</td>
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<td>Sykes et al, 2005</td>
<td>New Zealand</td>
<td>Retrospective review</td>
<td>15-19y</td>
<td>243 women aged 15-19y identified from colposcopy database of 1 hospital</td>
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<td>Massad et al, 2005</td>
<td>US</td>
<td>Retrospective analysis</td>
<td>14-19y</td>
<td>211 teenagers aged 14-19y referred to colposcopy for abnormal cytology</td>
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<td>Wright et al, 2005</td>
<td>US</td>
<td>Retrospective</td>
<td>12-18y</td>
<td>477 women 12-18y old, with 1st cytologic diagnosis. 422 with LSIL and 55 with HSIL identified from Washington University Hospital’s cytopathology database with follow-up information</td>
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**Abbreviations:** ASC-US: atypical squamous cells of undetermined significance; CIN: cervical intraepithelial neoplasia, HGSIL: high grade squamous intraepithelial lesions; FU: follow-up; LGSL: low-grade squamous intraepithelial lesions; y: years
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<td>Insinga et al, 2011</td>
<td>Various but most participants from North America, followed by South and Central America</td>
<td>Placebo arm of vaccine study</td>
<td>From 676 women aged 16 to 23, HPV16 infections were detected in 273 women and HPV18 infections in 113 women</td>
<td>Women underwent cytology and cervical swab for PCR testing for HPV types at 6 month intervals for up to 4 years. Most incident HPV infections cleared without detection of CIN at 36m (67.4% of HPV16 infections; 76.8% of HPV18 infections). Within 36m the probability of progression to CIN1 was 17.9%; to CIN2 7.6% and CIN3 1.7% for HPV16. For HPV18 the respective figures were 16.7%, 4% and 0%. Figures also provided for HPV31/33/35/45/52/58/59. Age-specific data was not provided.</td>
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<td>Brown et al, 2005</td>
<td>US</td>
<td>Prospective cohort</td>
<td>60 adolescents aged 14-17 years attending 1 of 3 primary care clinics</td>
<td>Girls were followed up for 2.2 years during which clinicians obtained cervical swabs and subjects themselves obtained vaginal swabs all tested for HPV. High risk HPV types were detected in 39% of specimens. During the study period 49/60 girls tested positive for HPV, cumulative incidence 82%. Median duration of persistence of HPV infection was 168 days. Abnormal cervical cytology results occurred in 37% of women but only 1 girl developed HGSIL abnormality during the study period. Age-specific data was not provided.</td>
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**Abbreviations:** CIN: cervical intraepithelial neoplasia, HGSIL: high grade squamous intraepithelial lesions; y: years
References


