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 <25years.

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

Author	Country	Study	Subjects	Findings
Saeed-Vafa et al, 2014	US	Retrospective review	92 women 14-20y identified from cytopathology database over 9y period (2001-2009)	Of 8011 women <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.
Castanon et al, 2013	UK	Audit	1800 women diagnosed with cervical cancer aged 20-29y, from 2007 to 2012 from the National Audit of Invasive Cervical Cancers	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 <25y having a stage 2 or worse, vs 6% in women ≥25y ($p<0.001$). A higher proportion of women 20-24y in comparison with older women were diagnosed with adenosquamous carcinoma and other rarer histological types (10% vs4%, $p<0.001$).

Bernard et al, 2012	US	Longitudinal data analysis	Data from 1999-2008 from 2 federal cancer surveillance programs covering 92% of the US population	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

Author	**Country**	**Study**	**Subjects**	**Findings**
International Collaboration of Epidemiological Studies of Cervical Cancer Studies	Multiple	Meta-analysis	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.	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)].
Louie et al, 2009	8 developing countries	Pooled IARC case-control studies	1864 invasive cervical carcinomas (ICC) and 1719 controls	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.
Moscicki et al, 2008	US	Prospective study	622 women 13-24y with abnormal cytology results of LSIL,HSIL, ASCUS/ hrHPV+ve, ASC-H (Years 2002-6)	CIN3 was found in 6.6% of the 622 women with abnormal cytology results and no cancers were detected. The authors state that the rate of CIN3 among this group of adolescents was less than half of that reported for adult females with abnormal cytology results (estimated to range between 10-16%).
Case et al, 2004	US	Retrospective review	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

	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

Author	Country	Study	Subjects	Findings
Wilkinson et al, 2015	New Zealand	Retrospective cohort	123 women <20y and 539 women ≥20y with a diagnosis of CIN1 or CIN2 (total n=662)	Women identified from database of 2 colposcopy units and follow-up data identified to determine recurrence of HG lesions. In the <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.
Moscicki et al, 2010	US	Prospective study	95 women aged 13-24y with histologically confirmed CIN2	Women were followed up at 4 month intervals. 38% cleared by 1 year, 63% by year 2 and 68% by year3. 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.
Monteiro et al, 2010	Brazil	Cohort study, partly retrospective and partly prospective	147 sexually active females 11-19 years old with cervical intraepithelial lesions	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 cytopathology 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 regressed while 3.1% progressed from CIN1 to CIN2/3.
Fuchs et al, 2007	US	Retrospective cohort	93 women <21y of which 12 were ≤16y, 38 were 17-19y and 43 were 20-21y) with biopsy confirmed CIN2, identified from colposc	5/12 women aged ≤16y were referred to colposcopy for HSIL, 5/12 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

			database	years of follow-up, 75% of women ≤16y experienced regression of their lesions.
Sykes et al, 2005	New Zealand	Retrospective review	243 women aged 15-19y identified from colposcopy database of 1 hospital	Of the 243 women, 2x15y olds were referred with LGSL/ASCUS, 11x16y olds with LGSL/ASC-US and 1 with HGSL and 30x17y olds with LGSL/ASC-US and 7 with HGSL. Following colposcopy, only one 17 year old girl had biopsy proven CIN3. 6x17y olds and 4x15y olds had biopsy proven CIN2. The authors state that screening teenage women results in invasive investigations and treatment without proven benefit.
Massad et al, 2005	US	Retrospective analysis	211 teenagers aged 14-19y referred to colposcopy for abnormal cytology	The group of women included of 2x14y olds, 18x15y olds and 23x16 year olds. After colposcopy and biopsy, CIN3 was confirmed in one 15 year old and one 16 year old, none of which were referred for HGSIL. CIN2 was found in 3x16y olds and 1x15y old while the other women had CIN1 or less. No cancers were found. HG lesions were confirmed in 15% of the 211 teenagers. Based on their results the authors question the utility of cervical cancer screening among teenagers.
Wright et al, 2005	US	Retrospective	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	The HSIL cohort included 1x 12 year old, 1x 13 year old, 1x 14 year old, 4x15 year olds, 7x16 year olds18x17 year olds and 23x18 year olds, After a median follow-up of 16m, 50.9% of the cases with an initial HSIL pap results were found to have a high-grade abnormality. After 12m within the study, 24% had biopsy confirmed CIN3 and after 36m the rate of progression to CIN3 increased to 31%. However, age-specific data was not provided.

Abbreviations: ASC-US: atypical squamous cells of undetermined significance; CIN: cervical intraepithelial neoplasia, HGSIL: high grade squamous intraepithelial lesions;; FU: follow-up; LGSIL: low-grade squamous intraepithelial lesions; y: years

Table 3: summary of studies reporting the natural history of cervical lesions in adolescents without abnormalities

Author	Country	Study	Subjects	Findings
Insinga et al, 2011	Various but most participants from North America, followed by South and Central America	Placebo arm of vaccine study	From 676 women aged 16 to 23, HPV16 infections were detected in 273 women and HPV18 infections in 113 women	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.
Brown et al, 2005	US	Prospective cohort	60 adolescents aged 14-17 years attending 1 of 3 primary care clinics	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.

Abbreviations: CIN: cervical intraepithelial neoplasia, HGSIL: high grade squamous intraepithelial lesions; y: years

References

Benard VB, Watson M, Castle PE, et al. Cervical carcinoma rates among young females in the United States. Obstet Gynecol. 2012; 120:1117–23.

Brown DR, Shew ML, Qadadri B, Neptune N, Vargas M, Tu W, Juliar BE, Breen TE, Fortenberry JD. A longitudinal study of genital human papillomavirus infection in a cohort of closely followed adolescent women. J Infect Dis. 2005 Jan 15;191(2):182-92.

Case AS, Rocconi RP, Straughn JM Jr, Wang W, Roark K, Waltman EE, Huh WK. Cervical intraepithelial neoplasia in adolescent women: incidence and treatment outcomes. Obstet Gynecol. 2006 Dec;108(6):1369-74.

Castanon A, Leung VM, Landy R, Lim AW, Sasieni P. Characteristics and screening history of women diagnosed with cervical cancer aged 20-29 years. Br J Cancer. 2013 Jul 9;109(1):35-41.

Fuchs K, Weitzen S, Wu L, et al: Management of cervical intraepithelial neoplasia 2 in adolescent and young women. J Pediatr Adolesc Gynecol 2007; 20:269.

Insinga RP, Perez G, Wheeler CM, et al: Incident cervical HPV infections in young women: transition probabilities for CIN and infection clearance. Cancer Epidemiol Biomarkers Prev 2011; 20:287

International Collaboration of Epidemiological Studies of Cervical Cancer. Cervical carcinoma and sexual behavior: collaborative reanalysis of individual data on 15,461 women with cervical carcinoma and 29,164 women without cervical carcinoma from 21 epidemiological studies. Cancer Epidemiol Biomarkers Prev. 2009 Apr;18(4):1060-9.

Louie KS, de Sanjose S, Diaz M, Castellsagué X, Herrero R, Meijer CJ, Shah K, Franceschi S, Muñoz N, Bosch FX; International Agency for Research on Cancer Multicenter Cervical Cancer Study Group. Early age at first sexual intercourse and early pregnancy are risk factors for cervical cancer in developing countries. Br J Cancer. 2009 Apr 7;100(7):1191-7.

Massad SL, Markwell S, Cejtin HE, Collins Y. Risk of high-grade cervical intraepithelial neoplasia among young women with abnormal screening cytology. J Low Genit Tract Dis. 2005 Oct;9(4):225-9.

Monteiro DL, Trajano AJ, Russomano FB, et al: Prognosis of intraepithelial cervical lesion during adolescence in up to two years of follow-up. J Pediatr Adolesc Gynecol 2010; 23:230

Moscicki AB, Ma Y, Wibbelsman C, et al: Rate of and risks for regression of cervical intraepithelial neoplasia 2 in adolescents and young women. Obstet Gynecol 2010; 116:1373

Moscicki AB, Ma Y, Wibbelsman C, et al: Risks for cervical intraepithelial neoplasia 3 among adolescents and young women with abnormal cytology. Obstet Gynecol 2008; 112:1335

Rissel C, Heywood W, de Visser RO, Simpson JM, Grulich AE et al. First vaginal intercourse and oral sex among a representative sample of Australian adults: the Second Australian Study of Health and Relationships. Sex Health. 2014 Nov;11(5):406-15.

Rissel CE, Richters J, Grulich AE, de Visser RO, Smith AM. Sex in Australia: first experiences of vaginal intercourse and oral sex among a representative sample of adults. Aust N Z J Public Health. 2003;27(2):131-7.

Saeed-Vafa D, Huang Y, Manucha V. Should cervical cancer screening begin at age 21 for everyone? A quantitative analysis in a high-risk, low-income, African American/Hispanic young-adult population. Diagn Cytopathol. 2014 Mar;42(3):205-12.

Sykes P, Harker D, Peddie D. Findings and outcome of teenage women referred for colposcopy at Christchurch Women's Hospital, New Zealand. N Z Med J. 2005 Mar 11;118(1211):U1350.

Wilkinson TM, Sykes PH, Simcock B, Petrich S. Recurrence of high-grade cervical abnormalities following conservative management of cervical intraepithelial neoplasia grade 2. Am J Obstet Gynecol. 2015 Jun;212(6):769.e1-7.

Wright JD, Davila RM, Pinto KR, Merritt DF, Gibb RK, Rader JS, et al. Cervical dysplasia in adolescents. Obstet Gynecol 2005;106:115–20.