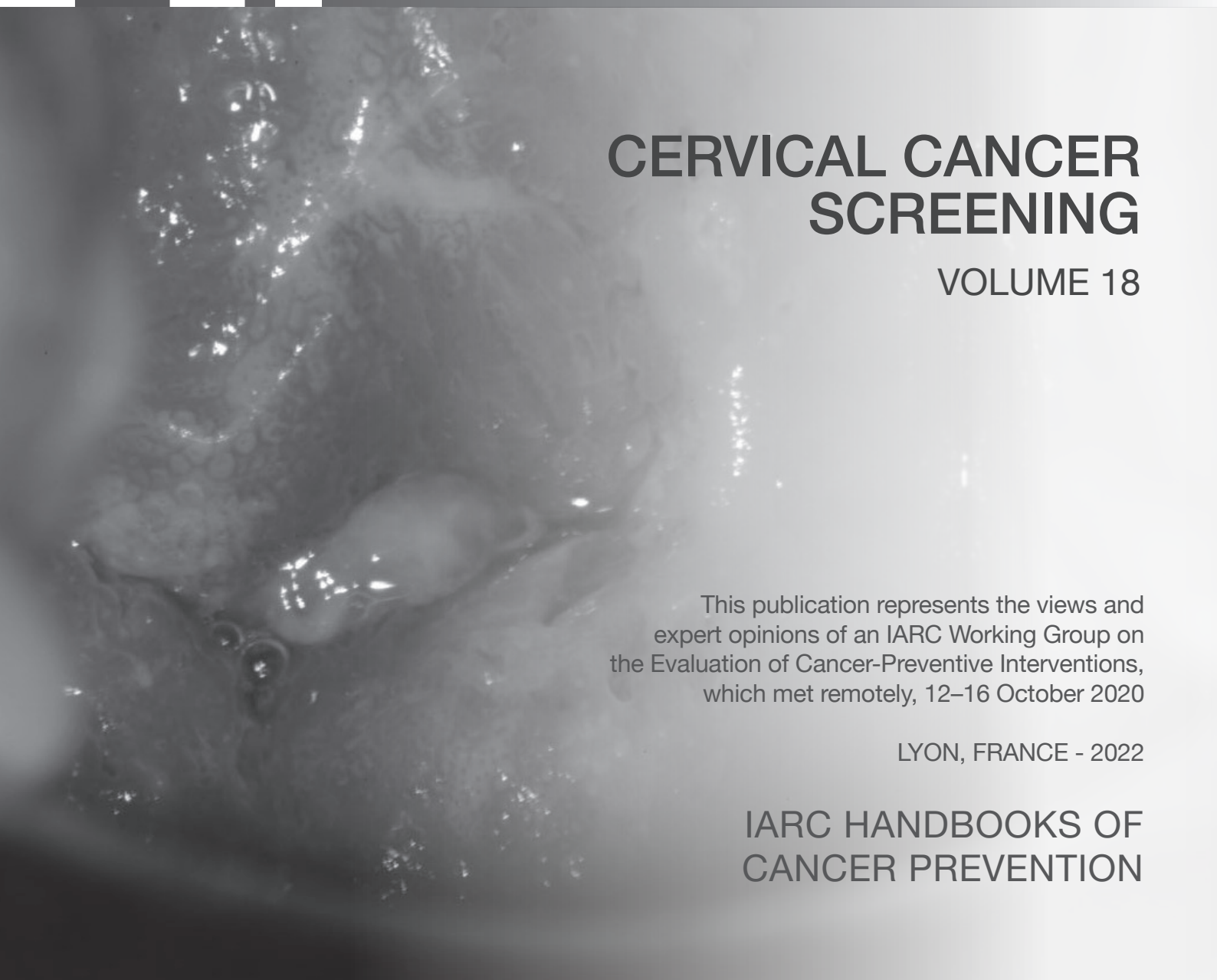
IARC HANDBOOKS



CERVICAL CANCER SCREENING

VOLUME 18

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IARC HANDBOOKS OF CANCER PREVENTION

International Agency for Research on Cancer

World Health Organization

Table 4.13 Case–control studies on the effectiveness of cervical cancer screening within service screening programmes using conventional cytology

Reference Outcome	Area, year programme began, screening age and interval, women included	No. of cervical cancer deaths, source, time period for cervical cancer deaths, years of diagnosis, proportion of eligible women included	Screening exposure Age of included women	No. of controls, source, whether same source population as cases, matching variables, alive at date of death or diagnosis of case	Linkage or use of screening, cancer registry, death databases, data items available	Adjustments	Cervical cancer incidence or mortality OR (95% CI)[a]	Comments
Makino et al. (1995) Invasive cervical cancer	Miyagi, Japan. Began 1984. Annual cytology from age 30 yr	198 invasive cervical cancer cases in 1984–1990. 129 mass screen-detected cases; 69 remaining cases were outpatients with gynaecological symptoms All eligible women were included Prior hysterectomy or abnormal cytology excluded	Measured by cytology files and questionnaire. Diagnostic smears excluded Age 35–79 yr	396 controls. 2 controls per case, matched on age (± 5 yr) and district of residence. For screen-detected cases, data were taken from screening files of other screened women; for outpatient-detected cases, data were sourced from outpatient gynaecologist files	Records of screening programme held on site. If questionnaire reported screening, accepted	None	Incidence: 0.14 (0.088–0.230)	Ever vs never screened Non-significant for adenocarcinoma (OR, 0.40; 95% CI, 0.091–1.753) No difference in effectiveness for age 34–49 yr vs 50–79 yr
Talbott et al. (1995)	Pennsylvania, USA. American Cancer Society recommendation: 3-yearly Pap tests at ages 20–65 yr	467 invasive cervical cancer cases from 1 July 1984 to 30 June 1985, identified through cancer registry. 53 of 467 (11.3%) excluded because not Black or White race, unknown race or stage, age > 80 yr or deceased at time of notification 149 cases included after pathology re- review and 2 partial interviews excluded 143 matched pairs (30.6% of original cases)	Questionnaire self-report to recall 10 yr of Pap test history Age 25–79 yr Smear test within 1 yr of diagnosis considered diagnostic	1 control per case on same street in neighbourhood matched on age (5-yr band) and race using telephone directories. Invited by letter, then telephone. Hysterectomy excluded. Of 231 eligible, 147 (64%) interviewed	Cases sourced from cancer registry	Marital status, income, visit to physician within 3 yr, smoking status, no. of pregnancies, age at first pregnancy, no. of long-term relationships, use of birth control, use of condoms	Incidence, no Pap test within 3 yr: 3.10 (1.45–6.64) [Unscreened reference group: 0.32 (0.15–0.69)]	Consent-based invitation via clinician who notified cancer registry and 1-h telephone interview 1.5–2 yr after notification. Of 414 age-eligible cases, 117 (28%) deceased. Of 297 alive, 52 (18%) could not be interviewed. Among women who could have been interviewed, 62% (153) of those with invasive cancer participated Selection bias resulted in overrepresentation of early-stage cancer compared with registry data Recall bias likely

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Zappa et al. (2004) Incidence	Florence, Italy. Area-organized screening since 1980. 3-yearly Pap tests	208 women aged ≤ 70 yr diagnosed with invasive cervical cancer in 1994–1999 and resident in area for ≥ 5 yr. Tuscany Tumour Registry. 71.1% SCC, 25.5% adenocarcinoma, 3.4% other	Computerized archive of screening tests and diagnostic tests from referral centre. Estimated to contain 2/3rds of all in region. Smear tests in 12 mo before diagnosis excluded Categorized as (a) ≥ 1 Pap test < 3 yr before the index date; (b) most recent Pap test 3 yr to < 6 yr before index date; (c) most recent Pap test > 6 yr before index date; (d) no Pap test recorded in database	832 controls (4 per case) matched on year of birth randomly selected from residential database. Resident for ≥ 5 yr, and no hysterectomy per screening or hospital records *n* = 832		Civil status, birthplace	OR by length of time since last test, all cancers: < 3 yr: 0.25 (0.15–0.42) 3–< 6 yr: 0.34 (0.21–0.56) ≥ 6 yr: 0.56 (0.38–0.82) Consistent and stronger effect seen for SCCs alone. Non-significant for adenocarcinomas alone Stronger effect seen for women aged ≥ 40 yr SCC, < 40 yr: 1 – < 5 yr: 0.32 (0.11–0.95) ≥ 5 yr: 0.51 (0.19–1.41) SCC, ≥ 40 yr: 1 – < 5 yr: 0.14 (0.07–0.27) ≥ 5 yr: 0.47 (0.29–0.77)	

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Andrae et al. (2008)	Sweden. Organized screening introduced between 1967 and 1977. Every 3 yr for women aged 23–50 yr and every 5 yr for women aged 51–60 yr	1230 cases. National audit of invasive cervical cancer cases from cancer registry, January 1999–December 2001, verified on pathology review Excluded smear test results in 6 mo before diagnosis	History from national screening registry for all cases and controls A woman was considered to have been tested within the recommended screening interval if she was aged ≤ 53 yr and had a smear taken 6–42 mo (0.5–3.5 yr) before a cervical cancer diagnosis; for women aged 54–65 yr, for whom a 5-yr screening interval applies, the smear had to be taken 6–66 mo (0.5–5.5 yr) before the cervical cancer diagnosis. Also assessed whether women aged ≥ 66 yr had had a smear test within 0.5–6.5 yr before a cancer diagnosis	6124 controls. No history of cervical cancer and alive at date of diagnosis of case. 5 age-matched from population register per case. Of 6150 potential controls, 26 excluded because of history of cervical cancer	Use of complete national registries for cancer and screening	Adjusted for age in birth cohorts	Not screened in recommended interval: 2.52, (2.19–2.91) [Unscreened reference group: 0.40 (0.34–0.46)] SCC: 2.97 (2.51–3.50) [SCC unscreened reference group: 0.34 (0.29–0.40)] Non-SCC: 1.59, (1.20–2.11) [Non-SCC unscreened reference group: 0.63 (0.47–0.83)]	No selection or recall bias because national registry data used. Risk consistent across age groups and also seen for non-SCC. Increased risk of advanced cancer OR presented by age, stage, and cancer type
Yang et al. (2008)	New South Wales, Australia. National programme since 1991. 2-yearly cytology, target population aged 20–69 yr	877 cases from New South Wales Cancer Registry diagnosed in 2000–2003 aged 20–69 yr	Screening history from registry assigned as none (no Pap test in the previous 4 yr), irregular (only 1 out of the previous 4 yr with a Pap test(s)), and regular	2614 controls (some removed because of hysterectomy). 3 matched controls from PTR, on register to 2004 not diagnosed with cancer 1996–2003, which holds records of all women who		Pap test result at the first index date Pap test in the 6 yr before the reference end-point was the main potential	[Results reported in article as RR even though they are modelled ORs] Compared with no screening in previous 4 yr: irregular screening, 0.18 (0.13–0.26); regular	Risk of bias towards screening because criterion for entry on PTR is ever screened. For the earliest index Pap test results, the proportion with a high-grade result was 6.4% of cases and 0.6% of controls. Almost 80% of controls had a negative

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			screening (≥ 2 Pap tests in the previous 4 yr) Pap tests 3 mo before diagnosis excluded as diagnostic	have ever been screened since 1996. Matched against death register to ensure alive at time of case diagnosis. Matched on age by month and year of birth		confounder; adjusted for in model	screening, 0.06 (0.04–0.09). If restricted to cases with any screening history (i.e. on PTR) to match selection criteria with controls, attenuated somewhat: irregular, 0.21 (0.15–0.30); regular, 0.07 (0.04–0.10)	Pap result for the earliest Pap test in the 6 yr, compared with 23% of cases Significant protection across all 10-yr age groups and for both SCC and non-SCC with both irregular and regular screening
Decker et al. (2009)	Manitoba, Canada. The study recommended 3 annual Pap tests, then 2-yearly screening, from age 18 yr	666 cases of invasive cervical cancer in women aged ≥ 18 yr diagnosed in 1989–2001 (and resident in 1984–2001) from Manitoba Cancer Registry	Pap test use taken from the Manitoba Physician Claims database. Estimated to capture 95% of Pap tests (misses public laboratory)	3343 controls (5 controls per case) sourced from universal health insurance registration file. Controls were matched on age and residence Exclusions: hysterectomy, cervical cancer, or other malignant cancer. Matched on area and age ± 1 yr	Manitoba Cancer Registry, Manitoba Health Insurance Plan registration, or Manitoba Physician Claims database. Used administrative data sets, not self-report, for all variables	Income	No Pap test in previous 5 yr: 2.77 (2.30–3.30) [Unscreened reference group: 0.36 (0.30–0.43)]	15% stage 1A included in analysis
Murillo et al. (2009)	Colombia. Programme since 1991	200 cases from 222 originally identified. Women in 4 Colombian provinces diagnosed with invasive cervical cancer aged 25–69 yr randomly selected from pathology records in 2005 Exclusions because of pregnancy in previous 3 yr, refusal to grant interview,	Structured survey of risk factors conducted by nurse. Blinded review of cytology histories. Symptomatic and follow-up tests after abnormal smears were excluded	200 controls of 206 originally identified, matched on age (± 2 yr) and neighbourhood from 4 Colombian provinces No cancer (verified by cytology) Excluded if hysterectomy, history of cervical cancer, or any physical or mental condition preventing completion of survey		Age at first intercourse, age at first birth, parity, OC use, no. of sexual partners, insurance status, literacy	No screen in previous 36 mo: 3.54 (2.01–6.24) [Unscreened reference group: 0.28 (0.16–0.50)]	

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		CIS not cancer, or residence outside of area						
Sasieni et al. (2009)	United Kingdom. Screening recommendations were local and either 3-yearly or 5-yearly		2 different measures of screening exposure: time since last negative result, and maximal screening interval (the longest period during the 6 yr before diagnosis in which the woman did not have a smear test)	6516 controls (~2 per case). Any other women registered with an NHS GP of a case were eligible. Randomly selected based on age and place of residence: 1 from same GP, 1 from another			Screening within 10 yr of diagnosis Adenocarcinoma: 0.72 (0.54–0.95) SCC: 0.37 (0.32–0.41) Adenosquamous: 0.25 (0.15–0.43)	Results also given by stage and by maximum interval, showing protection against stage 1B+ for SCC and adenosquamous but not adenocarcinoma. Significant protection from screening against stage 1B+ adenocarcinoma waned after a 2.5-yr interval
Kasinpila et al. (2011) Incidence	North-eastern Thailand (Khon Kaen Province). Cervical cancer screening programme established 2005. Pap tests for women at age 35, 40, 45, 50, 55, and 60 yr	130 cases. Women aged 30–64 yr diagnosed with invasive cervical cancer Conducted May–December 2009 in 4 tertiary hospitals. Residents aged 30–64 yr. Cases diagnosed within 3 mo before interview. 135 eligible, 130 participated. 77% SCC	Risk factors and screening history collected by structured interview Interval between the most recent test and date of diagnosis (or date of interview for controls) was grouped into 5 categories: (1) no Pap tests (never), (2) 6 mo, (3) 6–11 mo, (4) 12–35 mo, (5) ≥ 3 yr	260 controls. 2 groups: hospital controls (randomly selected from general wards; women with gynaecological diseases were excluded) and hospital patient companions (apparently healthy visitors). Frequency-matched on age within 10-yr age groups. Participation rates, 95% (130/137) and 93% (130/140)		Age at first intercourse, alcohol consumption, OC use	Excluding smears in 6 mo before diagnosis: for 1–5 tests, 0.45 (0.25–0.84; for ≥ 6 tests, 0.29 (0.11–0.82) Testing in past 1–2 yr: 0.27 (0.13–0.56) Testing ≥ 3 yr ago: 0.42 (0.20–0.88)	
Lönnberg et al. (2012)	Finland. Screening established 1963–1970. Every 5 yr for women aged 30–60 yr; some	1548 cervical cancer cases in Finnish Cancer Registry in 2000–2009. 2 declined consent for research use of data	Screening history from mass screening registry. Opportunistic screens outside programme not recorded	9276 controls (6 per case) from the population register, matched on birth year and month. Alive and had not been diagnosed	Linkage using unique personal ID between registries (the cancer registry and the screening registry)	A correction factor was estimated to account for self-selection bias by calculating ORs for	Association between cervical cancer and screening participation: 0.53 (0.46–0.62)	By age group, significant protection from 40 yr to 54 yr Protective effect across cancer types and stage

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	areas screen at 25 yr and 65 yr		Non-attender if diagnosis occurred < 5 yr after non-response to a programme invitation. Screen detection if date of diagnosis within 12 mo of a screening test that resulted in referral Interval cases were diagnosed after a negative or borderline screening test or > 12 mo after a positive screening test, but before the next programme invitation	with cervical cancer at the time of diagnosis of the case		those not responding to invitation compared with those who were not invited Corrected using self-selection bias factor 1.29 and attendance rate 0.71		
Nascimento et al. (2012)	Brazil. Programme since 1990. 3-yearly Pap tests after 2 annual tests with negative results	152 cases diagnosed between January 2007 and August 2012 at Nova Iguaçu General Hospital, a referral hospital for screened women. Histologically confirmed. Eligibility age 25–69 yr, resident in municipality ≥ 36 mo. Excluded if previous gynaecological cancer, terminal, or mental health issues prevented completion of survey	Informed consent. Survey collected variables on education level, income, marital status, race, age at menarche, age at first intercourse, age at first pregnancy, parity, number of partners, OC use, and smoking status. Asked if ever had a Pap test (preventive examination), how many in life, and how many in past 36 mo	169 controls aged 25–67 yr. Eligibility age 25–69 yr, resident in municipality ≥ 36 mo. Women accompanying patients admitted to the hospital. Excluded if hysterectomy or never sexually active, or gynaecological cancer or mental health disorder. Paired to case by age and municipality		Education level, age, municipality, tobacco use	≥ 3 Pap tests 36 mo before index date: 0.16 (0.074–0.384) 1 or 2 Pap tests, not significant: 0.67 (0.275–1.640)	

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		169 eligible, 7 excluded (5 terminal, 2 mental health), 7 died before interview, and 3 refused Total of 152 cases aged 25–68 yr. 90% SCC		Of the total controls, 6 were excluded because of hysterectomy, and 6 were lost				
Kamineni et al. (2013) Incidence	USA. Members of 2 integrated health-care delivery systems in Washington State, Idaho, and Oregon	69 cases of invasive cervical cancer diagnosed in 1980–1999 in women aged 55–79 yr while enrolled and with 7 yr of prior enrolment before date of diagnosis. Checked against tumour registry and local SEER registry	Reviewed medical records to obtain screening history in previous 7 yr and clinical history, cofactors, demographics Grouped into screen-detected vs clinically detected Estimated pre-invasive detectable phase and occult invasive phase; sought to identify screening in PIDP	208 controls (3 per case). No hysterectomy or cervical cancer. Matched on age and length of time enrolled in health-care plan		Age, smoking status	Screening in previous 1 yr: 0.23 (0.11–0.44)	Estimated large reduction in incidence in year after negative screen, falling thereafter to baseline at 5–7 yr
Lönnberg et al. (2013) Mortality	Finland. Screening established 1963–1970. Every 5 yr for women aged 30–60 yr; some areas screen at 25 yr and 65 yr	545 deaths registered as due to cervical cancer in 2000–2009. 39 cases excluded as screening exposure mapped to pre-1990 with no screening information. Included 506 cervical cancer deaths in 2000–2009 in Finland	Screening history from mass screening registry. Opportunistic screens outside programme not recorded Non-attender if diagnosis occurred < 5 yr after non-response to a programme invitation.	3036 controls, matched on age of diagnosis. 6 controls per case from the population register, matched on birth year and month. Alive and had not been diagnosed with cervical cancer at the time of diagnosis of the case	Linkage using unique personal ID between registries (the cancer registry and the screening registry)	Corrected using self-selection bias factor 1.45 and attendance rate 0.71	Effect of participation in index screening event: 0.34 (0.14–0.49)	No significant protective effect against adenocarcinomas

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			Screen detection if date of diagnosis within 12 mo of a screening test that resulted in referral Interval cases were diagnosed after a negative or borderline screening test or > 12 mo after a positive screening test, but before the next programme invitation Index screening event was defined as the last age-group invitation and possible screening test within the 66 mo before the diagnosis					
Castañón et al. (2014) Incidence	England and Wales. Recommended screening interval, 5 yr at ages 50–64 yr	1341 cases. Cases in England diagnosed between April 2007 and March 2012; cases in Wales diagnosed between January 2007 and December 2009. Registered with an NHS GP. Audit data set. Estimate includes 78% of cases in England in the period, because of delays in data entry	Smear records in cervical screening call–recall system (national registry). Includes all NHS and many private provider smear tests taken in United Kingdom since 1988 To exclude screen-detected cancers, the study excluded women (including controls) diagnosed at age 65.0–	2646 controls. Any other women registered with an NHS GP of a case were eligible. Randomly selected based on age and place of residence: 1 from same GP, 1 from another	Likely manual matching of records by local NHS administration database staff then identified		Screening interval < 5.5 yr compared with no screen at age 50–64 yr: 0.25 (0.21–0.30) Adequate negative screening aged 50–64 yr compared with no screening: 0.16 (0.13–0.19)	Demonstrated protection against SCC and adenocarcinoma: SCC > adenocarcinoma Protective effect waned with time since screening. More frequent screening than 5-yearly was no more protective, and even screening with 9–15 yr interval was protective Study estimated absolute risks after negative screens by

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		Women aged ≥ 60 yr on 1 January 1988 excluded because may not have been invited for screening; therefore, few participants aged > 80 yr	65.5 yr with a cytology test within 6 mo of case diagnosis Screening history at 50–64 yr in 4 categories: (1) adequate negative, (2) suboptimal negative, (3) abnormal screening, (4) no screening					extrapolating study sample to overall population
Rustagi et al. (2014)	Pacific Northwest, USA	39 cases. Women who died of cervical cancer aged 55–79 yr from 47 potentially eligible (4 no medical records, 3 care outside of health plan, 1 < 6 yr pre-diagnosis enrolment) Cases were identified in 1 of 2 health-care plans in 1980–2010 51% SCC, 31% adenocarcinoma, 10% undifferentiated, 5% unknown histology, 3% adenosquamous	Screening history from medical records. Only screening tests, not diagnostic, included. Covariates extracted were marital status, BMI, smoking status, race, parity, menopause, OC use, immunosuppression	80 controls sampled from health plan enrolees on date of diagnosis of cases, matched on health plan, age within 6 mo, and duration of health plan enrolment (same or longer than duration for cases by no more than 6 mo). Hysterectomy excluded	Cases were ascertained from the Cancer Surveillance System for Group Health enrolees (part of the National Cancer Institute's SEER) and from the Kaiser Tumor Registry for Kaiser Permanente Northwest enrolees	Smoking status, marital status, race or ethnicity	≥ 1 screens in previous 7 yr: 0.26 (0.10–0.63) Inclusion of all measured covariates did not alter the magnitude of the association: 0.26 (0.09–0.77)	HPV testing used to triage ASC-US only
Vicus et al. (2014)	Ontario, Canada	1052 cases. Women with cervical cancer aged 20–69 yr between 1 January 1998 and 31 December 2008 who died from cervical cancer during this period	Centrally held health records for all residents. Cytology database holds all smears except for those performed in hospitals. Estimated to	10 494 controls. Women without a diagnosis of cervical cancer between 1 January 1998 and 31 December 2008 who were alive on the date of death of the case. 10 per case,	Data were obtained from 4 sources: the OCR, CytoBase, OHIP, and RPDB. All linked by unique ID		Screening 3–36 mo before the date of diagnosis protective in all age strata ≥ 30 yr: OR, 0.28–0.60 ($P < 0.05$) in all strata	No protection for women aged < 30 yr could be because there is no effect, there is a small effect, or it is too rare to detect

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		Study was interested in impact of screening on age, and no overall all-age effect was reported	hold 87% of all smears in province Screening exposure identified through database or smear billing code in insurance database. Exposure defined as 3–36 mo before the index date, 37–60 mo before the index date, or > 61–120 mo before the index date Smears in the 3 mo before the index date were considered diagnostic	matched on year of birth and area-based income quintile. Sourced from RPDB. Must have continuous enrolment, and physician must send smear test histories to cytology database Excluded if previous cervical cancer or hysterectomy				
Vicus et al. (2015)	Ontario, Canada	5047 cases. New invasive cervical cancer cases between 1 January 1998 and 31 December 2008 in cancer registry. Continuous residence since 1995 Study was interested in impact of screening on age, and no overall all-age effect was reported	Exposure was defined as periods from the index date, categorized as (1) between > 3 mo and 36 mo before the index date, (2) 37–60 mo before the index date, (3) 61—120 mo before the index date, (4) never or > 120 mo before the index date	10 094 controls. 2 controls per case, matched on year of birth and income (as above). Continuous residence since 1995. Excluded if physician did not send cytology to database. Excluded if hysterectomy before index date	Data were obtained from 3 sources: the OCR, OHIP, and RPDB. All linked by unique ID		Significant protective effect of screening 3–36 mo before the index date seen only in these age groups: 40–44 yr, 0.82 (0.69–0.97); 50–54 yr, 0.59 (0.48–0.73); 55–59 yr, 0.52 (0.48–0.73); 60–64 yr, 0.59 (0.46–0.76)	Screening 3–36 mo before the index date is associated with cancer incidence in women aged 20–24 yr, 25–29 yr, and 30–34 yr, and the effect is not significant in women aged 35–39 yr, 45–49 yr, and 65–69 yr Screening 37–60 mo before the index date was significantly protective in women aged 45–59 yr only Screening 61–120 mo before the index date was not significantly protective in any age group

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Rosenblatt et al. (2016) Incidence	USA. Area covers 14% of population of USA serviced by 11 SEER registries in the states of Connecticut, Iowa, New Mexico, Utah, and Hawaii, 13 counties in western Washington State, and the metropolitan areas of Detroit, Atlanta, San Jose-Monterey, San Francisco, and Los Angeles Study focused on women aged ≥ 65 yr screened in 1991–1999. Screening not recommended for age ≥ 65 yr during this period if previously adequately screened (USPSTF), but was provided 3-yearly by the insurance	1267 invasive cervical cancer cases in women aged ≥ 65 yr, with Medicare in 1991–1999 and no other insurance	Pap test recorded on Medicare claims data in the 2–7 yr before index date of case (considered as PIDP, similar to study of Kamineni et al., 2013) Ages 65–100 yr Second analysis restricted to those aged ≥ 72 yr who were eligible/had data from the full period 1991–1999	10 137 controls (up to 8 per case), matched on age (± 2 yr) and geographical location, selected from a 5% sample of Medicare beneficiaries (pool, *n* = 89 208) without a diagnosis of cancer and no known hysterectomy during the study period. Randomized non-replacement selection	Used SEER–Medicare programme with matched data across cancer registry and claims data. Used cervical screening history and hysterectomy from Medicare data. Pre-1991 data not available for screening history or hysterectomy	Race, income, education level, geographical area Stratified by age	Having had a Pap test 2–7 yr before index date was significantly negatively associated with the development of invasive cervical cancer: OR adjusted for race, income, 0.64 (0.53–0.7); also adjusted for hysterectomy, 0.38 (0.32–0.46) Effective across all age groups: OR adjusted for race, income, hysterectomy: 65–74 yr: 0.24 (0.15–0.37) 75–84 yr: 0.44 (0.34–0.55) 85–100 yr: 0.44 (0.29–0.66) In second analysis for women aged ≥ 72 yr with complete data for exposure period, OR adjusted for race, income, 0.67 (0.55–0.81); also adjusted for hysterectomy, 0.42 (0.35–0.52)	Results may not be generalizable to screening all older women because screening was not recommended for all women and it is unknown why some women were offered or chose screening. Previous screening history unknown Note large effect of estimating and adjusting for prevalence of hysterectomy in controls

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Reference Outcome	Area, year programme began, screening age and interval, women included	No. of cervical cancer deaths, source, time period for cervical cancer deaths, years of diagnosis, proportion of eligible women included	Screening exposure Age of included women	No. of controls, source, whether same source population as cases, matching variables, alive at date of death or diagnosis of case	Linkage or use of screening, cancer registry, death databases, data items available	Adjustments	Cervical cancer incidence or mortality OR (95% CI)[a]	Comments
							When adjusted for hysterectomy, significant for all stages: Localized: 0.55 (0.42–0.75) Regional: 0.27 (0.20–0.39) Distant: 0.30 (0.16–0.58) When adjusted for hysterectomy, by histology: Squamous: 0.31 (0.23–0.40) Adenocarcinoma: 0.76 (0.53–1.10) Other: 0.36 (0.21–0.61)	
Lei et al. (2019)	Sweden. Organized screening introduced between 1967 and 1977. Every 3 yr for women aged 23–50 yr and every 5 yr for women aged 51–60 yr	338 cases. Women diagnosed with invasive cervical cancer in 2002–2011, from the Swedish Cancer Registry, after clinical review and histopathological review of 91% of 338 cases of ASC (49%) and RICC (51%)	Screening registry history for last 2 screening rounds, recorded as not screened, normal, or abnormal. Smears in 6 mo before index date considered diagnostic	9691 controls (30 controls per case) from population registry. Matched on age and incidence density. No hysterectomy or cancer. Alive in Sweden on index date	Use of complete national registries for cancer and screening	Education level, age	2 tests compared with none: ASC, incidence rate ratio, 0.22 (0.14–0.34); RICC, 0.34 (0.21–0.55) 1 test compared with none: ASC, incidence rate ratio, 0.39 (0.26–0.59); RICC, 0.69 (0.45–1.06)	Greatest effect for those aged 30–60 yr vs ≥ 60 yr, for later stage, and for 2 tests, seen across all RICC types and HPV-positive and HPV-negative (archived samples were typed)
Wang et al. (2020) Incidence	Sweden. Organized screening introduced between 1967 and 1977. Every 3 yr for those aged	4254 cases diagnosed in 2002–2011, from the Swedish Cancer Registry, after clinical review and	Screening registry history for last 2 screening rounds, recorded as not	120 006 controls (30 per case) from population registry. Matched on birth year. No hysterectomy or	Use of complete national registries for cancer and screening	Education level, age Adjustment for parity in sensitivity	No tests compared with last 2 rounds: 4.1 (3.8–4.5)	Confirms regular screening required for protection

Table 4.13 Case–control studies on the effectiveness of cervical cancer screening within service screening programmes using conventional cytology

Reference Outcome	Area, year programme began, screening age and interval, women included	No. of cervical cancer deaths, source, time period for cervical cancer deaths, years of diagnosis, proportion of eligible women included	Screening exposure Age of included women	No. of controls, source, whether same source population as cases, matching variables, alive at date of death or diagnosis of case	Linkage or use of screening, cancer registry, death databases, data items available	Adjustments	Cervical cancer incidence or mortality OR (95% CI)[a]	Comments
	23–50 yr and every 5 yr for women aged 51–60 yr	histopathological review of 91% of cases. 20% microinvasive, 40% localized, 40% advanced	screened, normal, or abnormal. Smears in 6 mo before index date considered diagnostic. For those aged 26–28 yr, 1 screening round	cancer. Alive in Sweden on index date		analysis; little difference	[Unscreened reference group: 0.24 (0.22–0.26)] If missed last screening round but was screened in round before: 2.4 (2.2–2.7) [Unscreened reference group: 0.42 (0.37–0.45)] If was screened last round but missed round before: 1.6 (1.5–1.8) [Unscreened reference group: 0.63 (0.56–0.67)]	Increasing risk for more advanced cancers if not screened. Higher risk for SCC than for adenocarcinoma Further analysis by screening results, and identified ongoing risk if previous abnormal even if next screen negative

ASC, adenosquamous cell carcinoma; ASC-US, atypical squamous cells of undetermined significance; BMI, body mass index; CI, confidence interval; CIS, carcinoma in situ; GP, general practice; HPV, human papillomavirus; ID, identification; mo, month or months; NHS, United Kingdom National Health Service; OC, oral contraceptive; OCR, Ontario Cancer Registry; OHIP, Ontario Health Insurance Plan; OR, odds ratio; PIDP, pre-invasive detectable phase; PTR, Pap Test Register; RICC, rare types of invasive cervical carcinoma; RPDB, Registered Persons Database; RR, relative risk; SCC, squamous cell carcinoma; SEER, Surveillance, Epidemiology, and End Results Program; USPSTF, United States Preventive Services Task Force; yr, year or years.

[a] Data as reported in source, with conversion to reference group of unscreened women where necessary to standardize comparison.

14

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