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## Impact of organized and opportunistic Pap testing on the risk of cervical cancer in young women – A case-control study from Finland

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### HIGHLIGHTS

- The effect of screening on the risk of cervical cancer diminishes by decreasing age.
- Data on opportunistic testing was also available.
- Under the age of 25 Pap testing appeared to have no impact.
- A clear preventive effect was observed among women tested at age 35–39 years.
- Organized screening is more effective than opportunistic testing.

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### ABSTRACT

**Objective.** Effectiveness of organized cervical cancer screening has been shown in several studies. However, screening among women aged <25 years has been suggested to have little or no impact on the risk of cervical cancer. Also the significance of opportunistic testing in preventing cervical cancer is unclear. The aim of this study was to clarify the effect of opportunistic testing and organized screening on the risk of cervical cancer among young Finnish women.

**Methods.** In the Finnish Cancer Registry there were 284 cervical cancer cases diagnosed and tested below the age of 40 in 2004–2009. Screening histories and data on opportunistic testing for these women and their 1698 age-matched controls were derived from databases of the Mass Screening Registry and The National Institute for Health and Welfare from 1997 onward. OR's and 95% CI's for the association of cervical cancer diagnosis and participation in organized screening and opportunistic testing were estimated using unconditional logistic regression. Results were corrected for self-selection bias and attendance rate.

**Results.** Among women aged under 25, OR of cervical cancer for any Pap test taken 0.5–5.5 years before diagnosis was 1.25 (95% CI 0.46–3.43). Attending only organized screening at age 25–39 resulted in OR 0.52 (0.36–0.77), attending only opportunistic testing in OR 0.86 (0.60–1.25) and attending both in OR 0.48 (0.29–0.79).

**Conclusion.** Opportunistic testing showed no clear additional benefit on preventing cervical cancer. The study also supports findings on a smaller effect of screening in younger age groups.

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### 1. Introduction

Effectiveness of organized cervical cancer screening has been shown in several studies [1] [2], [3], but it may be dependent on age. Screening under 30 years old women has been generally shown to have only little

impact on the risk of cervical cancer whereas a clear risk reduction has been observed in women aged 40 years or over [4–9].

A well-organized screening program is considered to be more effective in cancer prevention than opportunistic testing. Further, it results in lower costs and less harm [10], [2], [11]. In well-organized population-based screening, all women are followed from the invitation and test to the potential treatment, and all data of steps are registered. These data are essential for monitoring and evaluation of the quality and effectiveness of screening. In opportunistic testing, these benefits are often lost due to incomplete follow-up and lack of registration. Also the

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suitable age range and testing interval may not be clearly defined or followed.

A human papilloma virus (HPV) infection is a necessary factor in the development of precancerous epithelial lesions and further cervical cancer [12–14]. Both HPV infections and mild cell atypia are known to be very prevalent but also transient at young age [15–17]. Pap testing therefore detects a significant number of mild abnormalities and even precancerous lesions which are likely to be regressive [18]. Excessive testing at young age thus causes not only more unnecessary testing and related psychological stress but also overtreatment of precancerous lesions which increases the risk for treatment related complications in reproductive health [2]. In Finland extensive opportunistic testing practice is particularly common in young women with low risk of cervical cancer [19,20].

The aim of the study is to evaluate age-specific effects of Pap testing among women aged <40 years using registry-based case-control data. We also assess differences in the preventive effects of opportunistic and organized testing against cervical cancer.

## 2. Material and methods

The organized screening program for cervical cancer in Finland was initiated in 1963. Municipalities are responsible for organizing the screening and delivering the results to the national Mass Screening Registry. All women aged 30–60 years are invited to screening with personal letter every five years. Some municipalities have extended invitations to 25 and/or 65-year olds. Opportunistic Pap testing has emerged later, after the onset of the organized screening program, but is currently extensive.

All women aged 13–99 years diagnosed with cervical cancer in 2000–2009 were identified as cases from the Finnish Cancer Registry and their age-matched controls were retrieved from the Population registry [8]. Screening histories prior to cases' diagnoses for all invited cases and controls were obtained from 1991 onwards from the Mass Screening Registry for organized screening. These data were created in 2012

and included 1546 cases and 9276 controls [8]. For the current study, we linked these data with available data on opportunistic testing prior to cases' diagnosis from the research database collected and maintained by The National Institute for Health and Welfare (THL). The THL research database includes data from the Social Insurance Institution of Finland (1997–2008) with Pap smears reimbursed in the private sector covering the whole country. Other data sources of the THL database are regional: data from the Finnish Student Health Service (2000–2008) includes Pap smears taken in the student health care covering the university towns, and data from the Southern Finland, i.e. from Turku region (2002–2009) and the capital region (2000–2009), include Pap smears taken in the public primary health care services. Diagnostic Pap tests, i.e. tests taken within the six-month period before cases' diagnoses were excluded. All data were linked with unique personal identifier as a key.

We restricted the data to cases aged <40 years at the time of a preventive Pap test and their respective controls. The preventive Pap test was defined to take place at least six months before the diagnosis of cervical cancer. Only women with the latest invitation for organized screening in 1997 or later were included in the study due to lack of opportunistic data before that year. To ensure adequate screening history only cases diagnosed from 2004 onwards and their respective controls were included. Overall, our study included 284 cases and 1698 controls, altogether 1982 women (Fig. 1). Women under the age of 30 composed approximately 28% of the whole study population. There were only 23 cases tested under the age of 25 (Table 1). Among them, two cases were diagnosed under the age of 15 and rest of them over the age of 20. Subgroup analyses were performed by morphology (squamous cell carcinoma and adenocarcinoma) and stage (carcinomas with Figo stage at least IB).

We estimated the association between the risk of cervical cancer and protective Pap testing using unconditional logistic regression adjusted for year of birth. Pap smears taken during the same month were counted only once since subsequent tests were regarded as retests due to a failure in the previous test. We examined a time period of 10 years

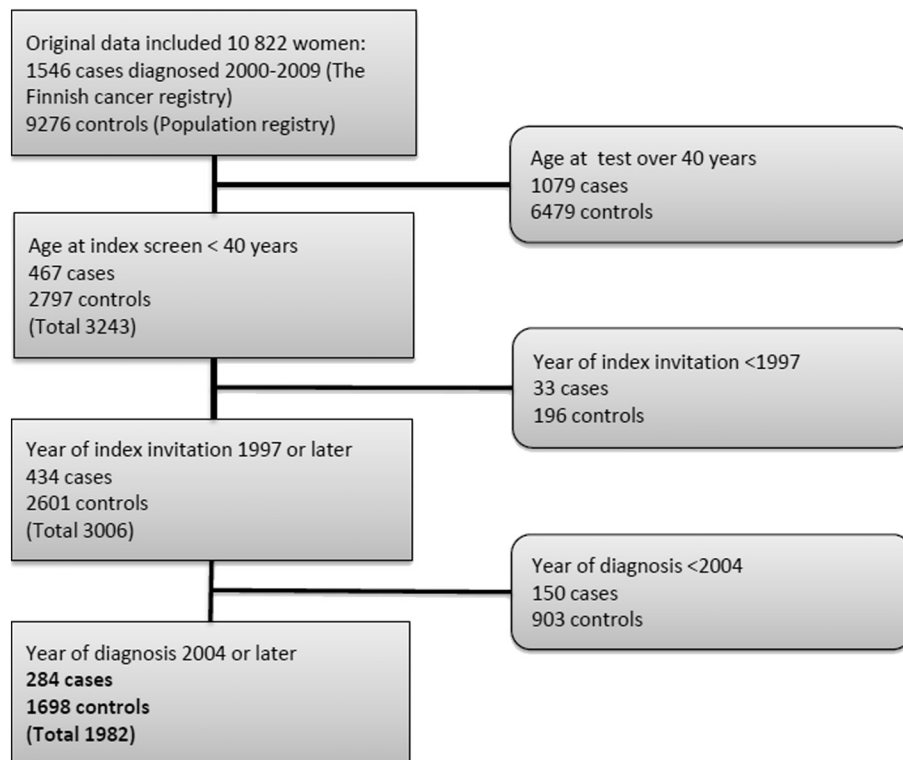


Fig. 1. Accumulation of cases and controls.

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