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Changes in cervical cancer incidence following the introduction of organized screening in Italy

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ABSTRACT

Objective. To quantify the impact of organized cervical screening programs (OCSPs) on the incidence of invasive cervical cancer (ICC), comparing rates before and after activation of OCSPs.

Methods. This population-based investigation, using individual data from cancer registries and OCSPs, included 3557 women diagnosed with ICC at age 25–74 years in 1995–2008. The year of full-activation of each OCSP was defined as the year when at least 40% of target women had been invited. Incidence rate ratios (IRRs) with 95% confidence intervals (95% CIs) were calculated as the ratios between age-standardized incidence rates observed in periods after full-activation of OCSPs *vs* those observed in the preceding quinquennium.

Results. ICC incidence rates diminished with time since OCSPs full-activation: after 6–8 years, the IRR was 0.75 (95% CI: 0.67–0.85). The reduction was higher for stages IB–IV (IRR = 0.68, 95% CI: 0.58–0.80), squamous cell ICCs (IRR = 0.74, 95% CI: 0.64–0.84), and particularly evident among women aged 45–74 years. Conversely, incidence rates of micro-invasive (stage IA) ICCs increased, though not significantly, among women aged 25–44 years (IRR = 1.34, 95% CI: 0.91–1.96). Following full-activation of OCSPs, micro-invasive ICCs were mainly and increasingly diagnosed within OCSPs (up to 72%).

Conclusion(s). Within few years from activation, organized screening positively impacted the already low ICC incidence in Italy and favored down-staging.

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Introduction

There is clear evidence on the efficacy of cytological screening in preventing invasive cervical cancer (ICC) (IARC, 2005). However, the continuous decline of ICC incidence rates observed in the last two decades was characterized by a strong heterogeneity among countries. In such context, areas with organized cervical screening programs (OCSPs) have experienced more marked decreases (IARC, 2005; Vaccarella et al., 2013; Bray et al., 2005a, 2005b). This general observation pointed to a greater effectiveness of OCSPs compared to opportunistic screening (*i.e.*, on women's own initiative) (Arbyn et al., 2008), which was also confirmed by the results of a case-control study in Finland (Nieminen et al., 1999).

Most findings on the impact of OCSPs derive from investigations conducted in areas without previous opportunistic activity, thus, data on the impact of OCSPs in populations already opportunistically screened are scanty (Quinn et al., 1999; Nygård et al., 2002; Simonella and Canfell, 2013; Taylor et al., 2006). A debate is presently ongoing about the opportunity of implementing organized programs, based on call–recall system and standardized quality assurance plans, in areas with already high Pap-smear testing coverage.

In Italy, an age-period-cohort analysis showed, between 1988 and 2002, a declining trend of the already low ICC incidence rates (Vaccarella et al., 2013). ICC incidence trends, however, were never assessed in relation with the introduction of OCSPs because of substantial difficulties. OCSPs were gradually introduced in Italy since the mid–late 1990s (Ronco et al., 2012a; Segnan et al., 2000), when opportunistic screening was already diffused (*e.g.*, the proportion of women aged ≥25 years who reported, in 1994, having ever had a Pap-smear in life was 52.2%) (ISTAT, 2005). Implementation was very progressive: OCSPs started their activity in different calendar years, and the time needed to invite the whole target population (*i.e.*, women aged 25–64 years) was heterogeneous and sometimes longer than the 3 scheduled years (Ronco et al., 2012a).

This study aims to assess the impact of OCSPs on ICC incidence in Italy comparing incidence rates, by tumor stage and histological type, in periods before and after full-activation of OCSPs.

Material and methods

This study is part of a population-based retrospective cohort investigation on the impact of OCPSs in Italian areas covered by cancer registration (Zucchetto et al., 2013a, 2013b). Briefly, the study considered all women diagnosed with ICC, in areas concurrently covered by population-based cancer registries (AIRTUM working group, 2009) and OCSPs (*i.e.*, 17 Italian areas covering about 31%, 23%, and 10% of the resident population in northern, central, and southern Italy, respectively). Cases identified on the basis of death certificates only (less than 0.5%), an indicator of poor data quality (AIRTUM working group, 2009), were excluded.

The present analysis focused on women diagnosed with ICC between 25 (*i.e.*, age at start of screening invitation) and 74 years of age (*i.e.*, 10 years beyond the last screening invitation age).

In addition to routinary variables (*e.g.*, age at diagnosis, year of diagnosis, residence area, and tumor histological type) (AIRTUM working group, 2009), cancer registries retrieved ICC stage specifically for this investigation. ICC histological types (coded according to the International Classification of Diseases for Oncology 3rd edition and to the World Health Organization classification) were categorized as 'squamous cell carcinoma', or 'adenocarcinomas' (including adeno-squamous) while ICC stage (coded according to the International Federation of Gynecology and Obstetrics, FIGO) as 'micro-invasive' (*i.e.*, stages IA, IA1, IA2) or 'fully-invasive' (*i.e.*, stages IB–IV).

Italian guidelines, largely based on the European ones, recommend OCSPs to actively invite resident women aged 25–64 years to undergo a free-of-charge Pap-smear, every three years. They also recommend that each program had a detailed protocol for the management of women with abnormal cytology and for treatment, which are integral components of the screening. A fail-safe system to assure implementation of such protocols is required, such as data registration, quality assurance and monitoring of all phases of the screening process. Surveys designed for monitoring OCSP activity and produce process indicators are indeed annually conducted (Ronco et al., 2012a).

As described elsewhere in detail (Zucchetto et al., 2013a), screening histories within OCSPs for women with ICC included in the study, were retrieved by record linkage with data of OCSPs and categorized as follows: women diagnosed in periods without OCSPs, diagnosed in periods with OCSPs but not yet invited to OCSPs, invited but having no cytology within OCSPs (*i.e.*, never compliant), having only negative cytologies within OCSPs (*i.e.*, non screen-detected), or having a positive/unsatisfactory cytology within OCSPs (*i.e.*, screen-detected).

Since OCSP implementation in Italy depends on regional authorities and local health units, screening activity started in different calendar years

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