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Cervical cancer screening in women vaccinated against human papillomavirus infection: Recommendations from a consensus conference

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ABSTRACT

In Italy, the cohorts of women who were offered Human papillomavirus (HPV) vaccination in 2007/08 will reach the age (25 years) for cervical cancer (CC) screening from 2017. The simultaneous shift from cytology-based screening to HPV test-based screening gives the opportunity for unprecedented reorganisation of CC prevention. The ONS (National Screening Monitoring Centre) Directive and the GISCi (Italian Group for Cervical Screening) identified the consensus conference as the most suitable method for addressing this topic. A summary of consensus recommendations is reported here. The main objective was to define the best screening methods in girls vaccinated against HPV and the knowledge required for defining evidence-based screening strategies. A Jury made recommendations about questions and proposals formulated by a panel of experts representative of Italian scientific societies involved in CC prevention and based on systematic reviews of literature and evidence. The Jury considered changing the screening protocols for girls vaccinated in their twelfth year as appropriate. Tailored screening protocols based on vaccination status could be replaced by "one size fits all" protocols only when a herd immunity effect has been reached. Vaccinated women should start screening at age 30, instead of 25, with HPV test. Furthermore, there is a strong rationale for applying longer intervals for re-screening HPV negative women than the currently recommended 5 years, but research is needed to determine the optimal screening time points. For non-vaccinated women and for women vaccinated in their fifteenth year or later, the current protocol should be kept.

Abbreviations: AIRTUM, Italian Association of Cancer Registries; AOGOI, Italian hospital obstetric gynaecologists Association; CC, cervical cancer; CI, Confidence Interval; CIN, Cervical Intraepithelial Neoplasia; DNA, Deoxyribonucleic acid; GISCi, Italian Group for Cervical Screening; hr HPV, high-risk Human Papillomavirus; HTA, Health Technology Assessment; IARC, International Agency for Research on Cancer; ICO, Catalan Institute of Oncology; ISTAT, The Italian National Institute of Statistics; IT, information technology; ONS, National Screening Monitoring Centre; PASSI, "Progressi dell'Aziende Sanitarie per la Salute in Italia" survey; PC, Promoter Committee; RR, Relative Risk; SIAPEC, Italian Society of Pathology and Diagnostic Cytology; SICi, Italian Society of Cytology; SICPCV, Italian Society of Colposcopy and Cervico-Vaginal Pathology; SIGO, Italian Society of Gynecology and Obstetrics; SItI, Italian Society of Hygiene, Preventive medicine and Public Health; TSC, Technical and Scientific Committee.

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1. Introduction

In Italy, in the near future the cohorts of women who were offered Human papillomavirus (HPV) vaccination will be reaching the age for screening for the precursors of invasive cervical cancer (ICC). This happens while screening is moving from being cytology-based to HPV-based. This situation represents a challenge but also an opportunity for unprecedented reorganisation of CC prevention (WHO/RHR, 2006).

In Italy, organised vaccination and cervical screening are managed by Regions, according to national prevention and vaccination plans. Current national screening guidelines recommend invitation for cytology-based screening every 3 years from age 25 to 30–35 years and for HPV-based screening every 5 years thereafter up to age 64. According to the national vaccination strategy, girls are invited for HPV vaccination during their 12th year of age. This strategy started in 2008, inviting the cohort of women born in 1996, who will reach 25 years - the age for being invited for screening - in 2021. In addition, some Regions adopted a multi-cohort vaccination strategy, vaccinating adolescents in their 16th or 18th year. The first of them are reaching 25 years in 2016, most will in 2018 (Giambi, 2014). Further details on the implementation of both programs are provided in Results (Question 1).

This new situation means that organised screening programs must review their strategies. In this context, providing regional decision makers (as it happened for HPV-based screening) with clear, practical and feasible national information, based on the best scientific evidence and defined with the participation of professional involved in the subject, is fundamental in order to standardise procedures throughout the country. Indeed, concerning HPV-based screening, a Health Technology Assessment report was published in 2012 on the basis of a systematic literature review about efficacy and undesired effects, conducted also in the frame of the preparation of EU guidelines (Ronco et al., 2012). It advised moving to HPV-based screening- and provided a detailed protocol. The national Ministry of Health (MOH) endorsed such conclusions in 2013. After direct evidence of greater efficacy of HPV-based screening in preventing ICC, (Ronco et al., 2014) the 2014 National Prevention Plan required a progressive shift to HPV-based screening within 2018 (AIRTUM, 2015).

A Consensus Conference was organised in 2015. Its main objective was to define the best screening methods in girls vaccinated against HPV and the knowledge required for defining evidence-based screening strategies. The Consensus Conference identified and defined the central and local actions to be implemented in order to optimise the integration of primary prevention programs with secondary prevention programs, as well as research activities connected with the knowledge needed for change.

A summary is reported here (Fig. 1).

2. Materials and methods

2.1. Consensus Conference organisation

The ONS (National Screening Monitoring Centre, a governmental agency supporting the MOH and local health authorities in screening implementation and monitoring) Directive and the GISCi (Italian Group for Cervical Screening, the scientific society of Italian organised cervical screening programmes) Coordination Committee defined the general aim and identified a Promoter Committee.

The Promoter Committee, including four technical experts from ONS and GISCi, identified the Consensus Conference model (Supplementary Figure), developed by the national system for guidelines (http://www.snlg-iss.it/), as the most suitable method. The Promoter Committee appointed a Scientific Committee (SC), including experts, and a Jury, including experts and stakeholders.

The Technical Scientific Committee defined the objective and scope. Then it collected and summarised available evidence. Work packages were assigned to TSC members or to external experts, identified by their recent research. A pre-conference document with questions (see Table 1), proposed solutions (see Table 2) and the evidence supporting the proposed solutions was prepared.

For each question the Jury expressed an answer, which could be:

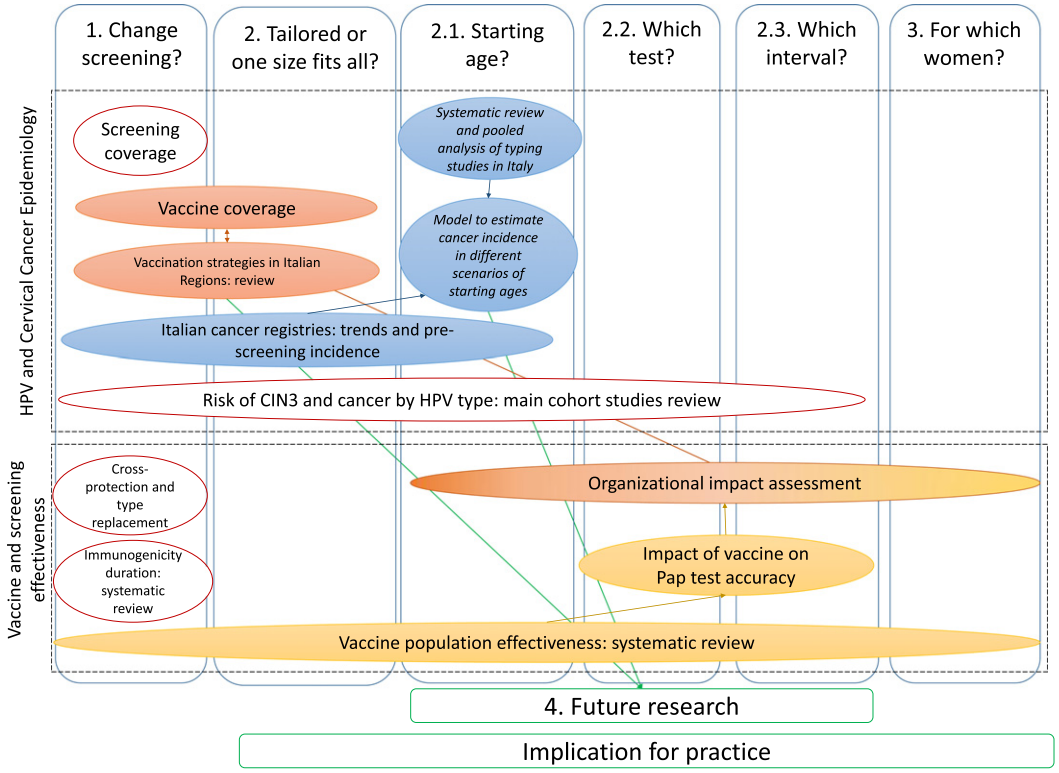

Fig. 1. Contribution of the work packages to the evidence supporting screening recommendations for the individual questions posed.