Human Papilloma Virus (HPV) vaccination in Italy: towards new perspectives and new challenges

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Human Papilloma virus (HPV) is the cause of a sexually transmitted infection which can lead to the development of genital warts, anogenital and oropharyngeal cancers. In Europe, about 90% of HPV-related cancers and 90% of genital warts are estimated to be vaccine preventable each year [1]. In Italy, around 5,000 cases of cancers are due to HPV infections each year [2]. This explains why HPV infection control is considered a public health priority.

Since 2017 the World Health Organization has recommended to include HPV vaccination in national immunization programs (NIP). The primary target of vaccination is represented by females 9-14 years old, ideally before sexual debut. Secondary targets, such as females >15 years old, males and other high-risk individuals (e.g. HIV) could be also considered whether affordable and sustainable, although the most important goal is achieving high vaccination coverage in girls [3]. From this perspective, Australia represents a virtuous example as vaccination coverage is above 80% for girls and 75% for boys. Indeed, a recent modeling study has showed that cervical cancer is expected to be almost eradicated by 2066 assuming the maintenance of this vaccination coverage and a 5-yearly HPV testing for cervical cancer screening [4].

In Italy, vaccination is recommended and freely offered to all young girls aged 11 years since 2008, but a relevant step forward was made only in 2017 with the National Vaccine Prevention Plan (PNPV) 2017-2019. In fact, the PNPV extended vaccination to boys in the twelfth year of life, men who have sex with men (MSMs) and immunocompromised patients (e.g. HIV) [4]. These new recommendations are aligned with the recent evidence about the cost-effectiveness of HPV vaccination in other targets [5, 6].

Furthermore, unlike other countries, the PNPV suggested to extend vaccination to women aged 25 years at the moment of cervical cancer screening. Nonetheless, whether this strategy could be cost-effective is debating [5]. In fact, albeit the nonavalent HPV vaccine is approved for use up to 45 years old, many countries do not offer vaccination in older women. For example, Australia does not support vaccination over 19 years of age because people are likely to have been already exposed to HPV infection through sexual activity and vaccine would be less effective [7]. USA consider vaccination up to 21-26 years old, but for MSMs [8] and UK offers free vaccination up to 45 years just to MSMs and transgenders [9]. Nevertheless, the extension of vaccination to age groups other than adolescents could provide an important opportunity to achieve those who missed the vaccination in earlier ages and could counter the unsatisfactory Italian levels of vaccination coverage. In fact, the goal set by the PNPV is to achieve a 95% vaccination coverage, but a decreasing trend over time has been reported in Italy with latest full-course vaccination coverage being as low as 50% among females and nearly 20% among males. Furthermore, important regional differences emerged, with one-dose coverage ranging from 40.6 to 81.1% among females and from 0 to 64.8% among males and full-course coverage ranging from 23.3 to 75.5% and from 0 to 60.0% respectively [11].

There are several contextual factors which hinder an effective vaccination offer and uptake. First of all, the presence of

several Italian health regional systems. Secondly, there are not national directives suggesting the best strategies to ameliorate vaccine acceptance, guarantee equity and eventually increase coverage. A first attempt to disentangle this matter was made in 2013 by the Valore Project [12]. The project identified several critical actions that can impact on HPV vaccine delivery such as education of healthcare workers, promotion of information events in schools, empowerment of vaccine services as reference points for vaccinations, both for the population and for local health workers, offer of integrated vaccination for adolescents and many others. It was a relevant starting point but there still be the need for identifying best practices to successfully outreach the target population. Academic and grey scientific literature is plenty of evidence about such strategies. For instance, Australia is known to use a school-based delivery program and to be supported by a HPV national register that collects data and sends reminder notices and completion statements to vaccinated persons [7] and USA have settled and tested several strategies to implement HPV vaccination coverage. This evidence could support future nationwide initiatives to increase vaccination coverage, which remains a crucial issue in Italy.

In conclusion, although Italy was among the first countries to launch a national HPV campaign and to extend HPV vaccination to other target populations, coverage is still low and this makes it essential to identify best practices that could successfully tackle the problem. Furthermore, future research should focus on the value of vaccination in older age groups and in other specific targets such as women treated for high-grade cervical diseases for which vaccination is expected to decrease the recurrence of disease.

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