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Human papillomavirus vaccination coverage in Luxembourg – Implications of lowering and restricting target age groups

Ardashel Latsuzbaia [a,*], Marc Arbyn [b], Steven Weyers [c], Joël Mossong [a]

[a] Epidemiology and Microbial Genomics, Laboratoire National de Santé, 1 rue Louis Rech, L-3555 Dudelange, Luxembourg
[b] Unit of Cancer Epidemiology, Belgian Cancer Centre, Scientific Institute of Public Health, Rue Juliette Wytsman 14, 1050 Ixelles, Belgium
[c] Department of Obstetrics and Gynecology, Ghent University Hospital, De Pintelaan 185, 9000 Gent, Belgium

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ABSTRACT

Background: In Luxembourg, a national Human Papillomavirus (HPV) vaccination programme was introduced in 2008, targeting 12–17 year old girls offering a choice of bivalent or quadrivalent vaccine free of charge. In 2015, the programme was changed offering the bivalent vaccine only to 11–13 year old girls. The aim of this study was to evaluate the HPV vaccination coverage, to assess the impact of age target changes and compare vaccination coverage to other European countries.

Methods: Anonymous HPV vaccination records consisting of individual vaccine doses obtained free of charge in pharmacies between 2008 and 2016 were extracted from the Luxembourgish Social Security database. Additional aggregate tables by nationality and municipality were analysed.

Results: Of the target cohort of 39,610 girls born between 1991 and 2003 residing in Luxembourg, 24,550 (62.0%) subjects obtained at least one dose, 22,082 (55.7%) obtained at least two doses, and 17,197 (43.4%) obtained three doses of HPV vaccine. The mean age at first dose was 13.7 years during 2008–14 and 12.7 years in 2016 after the age target change. Coverage varied significantly by nationality ($p < 0.0001$): Portuguese (80%), former Yugoslavs (74%), Luxembourgish (54%), Belgian (52%), German (47%), French (39%) and other nationalities (51%). Coverage varied also by geographical region, with lower rates (<50%) noted in some Northern and Central areas of Luxembourg (range: 38% to 78%).

Conclusion: Overall HPV vaccination coverage in Luxembourg is moderate and varied by nationality and region. The policy changes in 2015 did not have a substantial impact except lowering age at initiating vaccination. Options to improve coverage deserve further investigation.

1. Introduction

The recognition that cervical cancer is etiologically linked with persistent human papillomavirus (HPV) infection, [1,2] has led to the development of various cervical cancer preventive programmes, including screening and vaccination [3]. In 2006, the first HPV vaccine (Gardasil) was approved in the United States and the European Union [4]. This quadrivalent vaccine targets genotypes 6, 11, 16 and 18. Genotypes 16 and 18 account for approximately 70% of all cervical cancers, whereas genotypes 6 and 11 are the main cause of genital warts [5–7]. In 2007, a bivalent HPV vaccine (Cervarix) was introduced to the market for the primary prevention of genotypes 16 and 18. Since 2015, a nonavalent vaccine (Gardasil 9) has become available in Europe targeting nine HPV genotypes (6, 11, 16, 18, 31, 33, 45, 52, 58) [8]. By 31 March 2017, globally 71 countries have introduced national HPV vaccination programmes including 26 countries in Europe [9]. By the end of 2014, 47 million female subjects received HPV vaccines worldwide [10]. Recent studies show a significant reduction of vaccine-associated genotypes and protection from cervical lesions in vaccinated girls [11–14]. Several countries reported a decrease in incidence of genital warts following the introduction of national HPV vaccination programmes [15–17]. Moreover, the significant reduction of genotypes 31, 33, and 45 not contained in vaccines suggests a degree of cross-protection [12,18–20]. HPV vaccination has the potential to prevent cervical cancer and related deaths worldwide [21].

In Luxembourg, the national HPV vaccination programme started in March 2008 targeting 12–17 years old girls [22]. The programme aimed to deliver three doses, ideally, before the onset of sexual activity. When girls were 12 years old, they automatically received an information letter from the National Health Insurance and a brochure advising them to get vaccinated by their physician

* Corresponding author at: Epidemiology and Microbial Genomics, Laboratoire National de Santé, 1 rue Louis Rech, L-3555 Dudelange, Luxembourg.
E-mail address: ardashel.latsuzbaia@lns.etat.lu (A. Latsuzbaia).

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of choice prescribing either bivalent or quadrivalent vaccine. An invitation letter and information brochure were provided in four languages (Luxembourgish, German, French and Portuguese). Vaccines were typically administered as three intramuscular injections over 6 months. The parents then collected the prescribed vaccine doses from the pharmacy free of charge.

Following the updated 2014 WHO/EMA recommendation [23], during the spring of 2015, the national vaccination policy was changed limiting vaccination to girls aged 11–13 years with two doses of bivalent vaccine over a 6 month interval. Girls aged 14–17 years were still eligible to receive three doses of bivalent or quadrivalent vaccine free of charge until the end of 2015.

The main purpose of this study was to evaluate the HPV vaccination coverage in Luxembourg based on the analysis of National Health Insurance records and compare it to the situation of countries in Europe with a similar health system.

2. Materials and methods

2.1. Study population

The study was performed using the Luxembourgish Social Security database, covering approximately 95% of the resident population, the remaining fraction consisting mainly of European Union institutions employees and their family members, which have their own social security system. The information contained in the database consists of patient characteristics, medical consultations, interventions, prescriptions, laboratory tests and hospital discharge data.

2.2. Data extraction and pseudonymisation

HPV vaccination records consisting of individual vaccine doses obtained in pharmacies between 2008 and 2016 were requested from the Social Security Inspection (http://www.mss.public.lu/acteurs/igss/index.html) who have direct access to the database. For data protection purposes, the Social Security Inspection changed personally identifiable social security numbers to pseudonymised identifiers for the study investigators so that no further linkage to other health information was possible. The data set in comma separated text format was transferred from the Social Security Inspection to the study team by secure file transfer.

2.3. Characteristics of the dataset

The data set analysed in this study consisted of pseudonymised personal identifiers, age at first vaccine dose acquisition, interval in days between first, second and third dose, year of birth, calendar year of obtaining the first, second and third dose, vaccine type, medical speciality of the prescribing physician and total number of doses obtained. For reasons of data protection only aggregate tables by nationality and municipality could be obtained. Nationality here refers to the nationality information recorded in the national registry of physical persons at the time of data extraction. In Luxembourg, nationality concept refers to citizenship. Additionally, we received the following socioeconomic data aggregated at commune level from the public statistics portal (http://www.statistiques.public.lu/): average monthly income, unemployment rate and frequency distribution of nationalities.

2.4. Statistics

Statistical analysis was performed in Stata 14.0 (StataCorp, USA). We used Pearson's correlation coefficient to assess the association between continuous variables. For the coverage calculations girls born after 2004 year were excluded from the analysis, since they had potentially not yet completed the full vaccination schedule.

2.5. Ethics and data protection

The study was approved by the National Research Ethics Committee (CNER 201501/02) and the National Data Protection Commission (CNPD 288/2016).

3. Results

At the end of 2016, 39,610 females born between 1991 and 2003 years were resident in Luxembourg according to the Social Security database.

3.1. Vaccination coverage

Of that cohort 24,550 (62.0%) obtained at least one dose of HPV vaccine, 22,082 (55.7%) obtained at least two doses, and 17,197 (43.4%) obtained three doses. 70.0% of girls initiating vaccination completed a full schedule with three doses and 89.9% completed a partial schedule with two doses. The lowest vaccination coverage with at least one dose was observed in girls born in 1991, significantly increasing in the following birth cohorts. The highest vaccination coverage was noted for the cohort born in 1998, with at least one, two and three dose coverages of 70.1%, 64.5% and 58.1%, respectively (Fig. 1).

3.2. Vaccine uptake over time

The total number of obtained vaccines per year varied substantially over time. It was highest in the first year after vaccine introduction, then stabilized until the policy changes in 2015 produced another substantial increase (Fig. 2a). Approximately half of the women born between 1991 and 1996 obtained their first dose in 2008 (Fig. 2b). The high vaccination uptake during the first year was due to larger number of age groups eligible for the first time (Fig. 2b). Despite the reduced target age range in 2016, the total number of girls initiating vaccination was similar to 2014 (Fig. 2).

3.3. Vaccination coverage by region and nationality

Coverage varied geographically ranging from 38.4% to 78.6%, and was lower in the North and Centre of Luxembourg. Communes with the highest coverage are located in the Eastern and Southwestern parts of the country (Fig. 3). Coverage was found to be significantly associated with nationality ($p < 0.0001$), highest for Portuguese (80%) or former Yugoslavs (74%), intermediate in

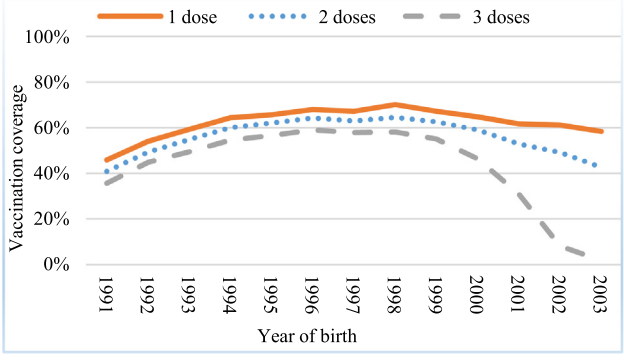

Fig. 1. HPV vaccination coverage per birth cohort.