Is EU/EEA population protected from polio?

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The WHO European Region has been declared polio-free since 2002. By 2010, inactivated polio vaccine (IPV) was the only polio vaccine in use in the EU/EEA for the primary vaccination of children. A systematic review of the literature on polio seroprevalence studies, complemented by the analysis of available vaccine coverage data, has been carried out with the aim of assessing the level of protection against polio in the European population. A total of 52 studies, with data from 14 out of the 31 EU/EEA countries, were included in the analysis. This systematic review shows that, overall, seroprevalence for PV1 and PV3 is high in most countries, although seroimmunity gaps have been detected in several birth cohorts. In particular, relatively low immunity status was found in some countries for individuals born in the 60’s and 70’s. Discrepancies between reported vaccination coverage and immunity levels have been also highlighted. Countries should make sure that their population is being vaccinated for polio to reduce the risk of local poliovirus transmission in case of importation. Moreover, assessing immunity status should be priority for those traveling to areas where wild polioviruses are still circulating.

Introduction

The WHO European Region has been declared polio-free since 2002. As a consequence, those member states of the European Union (EU) and the European Economic Area (EEA) that still included oral polio vaccine (OPV) in the childhood immunization schedule progressively switched to an inactivated polio vaccine (IPV) schedule. By 2010, IPV was the only polio vaccine in use in the EU/EEA for the primary vaccination of children, while OPV is still in use in Poland as a booster dose at 6 years of age. This was in line with the WHO global strategy to limit the circulation of vaccine-derived poliovirus once the circulation of wild-type poliovirus (WPV) had been stopped. Out of the 3 serotypes, only wild poliovirus 1 and 3 still circulate globally; the most recent wild poliovirus 3 detection was in November 2012, while poliovirus 1 is the predominant circulating wild strain.

The uncontrolled transmission of polio virus in Pakistan, as well as the increased international spread during the low season in 2014, led the Director-General of the WHO to declare, in May 2014, the international spread of WPV in 2014 a Public Health Emergency of International Concern (PHEIC), in accordance with the International Health Regulations (IHR).

The likelihood of WPV transmission and disease after importation into EU countries is considered low thanks to effective vaccination programmes and very good hygiene levels. Nevertheless, the changed global situation together with the presence of pockets of under-immunized population groups provides grounds for questioning this assumption.

As shown in the past and, most recently, by the detection of wild poliovirus type 1 (WPV1) from sewage samples collected in May 2013 in Israel and in March 2014 in Brazil, importation of poliovirus to polio-free regions may happen at any time as long as poliovirus is circulating in the world.

Knowledge of the immunity status of the population is a necessary component for assessing the risk of WPV transmission after importation into EU. In order to describe the susceptibility to polio in the EU, we conducted a systematic review of the literature on polio seroprevalence studies and complemented that information by estimating the number of susceptible individuals using available vaccine coverage data.

Methods

Search strategy and selection criteria

PubMed®, Embase.com® and Cochrane Library® have been searched up to 31st May 2014 for studies on the seroepidemiology of polio. The concepts of polio and seroprevalence, serology, immunity and prevalence were combined. Free-text/natural vocabulary (i.e. keywords) and medical subject heading (MeSH and Emtree) terms were used. No language or geographical restrictions were applied in the search string. Reference lists of retrieved articles were also reviewed.

References retrieved were uploaded to Endnote X6 (Thomas Reuter, 2012. Endnote X6.0.1. Philadelphia). Three investigators (D.N., A.M., P.C.S.) systematically screened search results by title and abstract. Exclusion criteria were: studies performed in non-EU/EEA or European overseas countries and territories, not polio, not in humans, no seroprevalence, clinical trial, outbreak
situation, missing information on age of study population, only data on immigrants and study performed before vaccination era. Full text articles of selected abstracts were retrieved and data extracted (D.N.) if they met the criteria. Discrepancies were resolved by consensus.

Data extraction and measurement of the outcome

Information on country, region, study population, study year, randomization, sample size, measurement tool, age, seroprevalence rates per serotype per age group and vaccine schedule was extracted. Data on infants less than one year were excluded due to potential confusion with maternal antibodies.

To measure immunity to polio, WHO recommends using a micro neutralization test with Sabin strains of poliovirus types 1 (PV1), 2 (PV2), and 3 (PV3) as challenge samples. In particular, the strains PV1-LSc/2ab, PV2-P712 and PV3-Leon as strains from which the Sabin oral vaccine were derived, and the strains PV1-Mahoney-Brunhilde, PV2-MEF-1 and PV3-Saukett as strains from which the Salk inactivated vaccine were derived. The cut off titer recommended by the WHO to demonstrate poliovirus immunity in humans is ≥1:8, however less conservative titres were also included (e.g. ≥1:2). We define high immunity when at least 90% of the population is immune to polio.

Data analysis

Seroprevalence by year of birth, starting from the onset of vaccination programmes in each country, has been calculated. To do so, age groups were recoded to birth cohorts by subtracting the age of the participants from the study year. When the study year was unknown, year of publication minus 1 was used. After recalculating the birth cohorts, the median (and range if more than one study was available) seroprevalence per decade was calculated by polio type and country. Some papers reported data from populations samples tested in different periods; in such cases the different evaluations are displayed as different studies (Table 1). Since the main goal of the study was to assess the risk for WPV reintroduction in Europe and wild type PV2 is no longer circulating, only data for PV1 and PV3 are presented.

To obtain coverage data on 3 doses of polio vaccine the Centralized Information System for Infectious Diseases (CISID) has been used (data available from 1980). Median coverage by decade and country has been calculated. Only countries for which we had data on seroprevalence were included. As vaccine effectiveness for 3 doses of either IPV or OPV is close to 100%, vaccination coverage was considered a good proxy of seroprevalence, hence vaccine coverage data were not adjusted.

Results

A total of 52 studies, with data from 14 out of the 31 EU/EEA countries, were included; these 14 countries account for around 80% of the EU/EEA population. The flow diagram of the study selection process can be found in Figure 1. All included studies used the (micro) neutralization test for determining immunity to poliovirus; 20 four studies used the cut off titer recommended by the WHO (≥1:8) and 6 used a more conservative cut off (≥1:10, and one ≥1:16) (Table 1). Concerning the Sabin strains of poliovirus used as challenge samples, 4 studies used the 3 Sabin strains corresponding with OPV (PV1-LSc/2ab, PV2-P712, PV3-Leon); 15 studies used the 3 inactivated polio virus strains (PV1-Mahoney-Brunhilde, PV2-MEF-1, PV3-Saukett); 3 studies used a combination of these strains and for 30 studies it was unknown; 22 studies did not report any information on cut off titer.

Seroprevalence for PV1 (Fig. 2) in the studies ranged from 57.8% in Belgium to 100% in Bulgaria and the Czech Republic. Most of the studies show PV1 seroprevalence over 80% for all the time periods available. However, for individuals born in the sixties and seventies, some countries reported lower PV1 seroprevalence values (when several estimates were available, the lowest value has been reported) (Belgium 57.8% (60s); Germany 62.4% (60s); Italy 65% (60s) and UK 64.4% (70s)). Concerning PV3 (Fig. 3), seroprevalence ranged from 61.4% in Belgium to 100% in Bulgaria and Czech Republic. Overall, seroprevalence for this serotype is over 80% in most of the studies. Also for PV3, some countries reported low seroprevalence values in individuals born in the sixties, seventies and eighties (Belgium 61.4% (60s); Germany 47.5% (80s); Italy 65.5% (60s–90s); Portugal 63.5% (80s) and UK 48.6% (60s)). Data on polio vaccine coverage (Figs. 2 and 3) ranged from 25% in the eighties in Portugal to 99.2% in the nineties in Sweden. Overall, reported vaccine coverage was very high, with all countries being over 90% after the nineties. In some countries like Germany, Italy and the UK, differences were found in the estimates produced by the different studies available (Table 2, Figs. 1 and 2).

In most countries where both seroprevalence and coverage data was available for the last decades, values were similar. For PV1, there is a slight difference of around 10% in Bulgaria and Germany in the nineties (Fig. 2). For PV3, differences between both data sources can be seen in Bulgaria, Germany, Greece -both in the eighties and the nineties- and for the last decade in the Netherlands (Fig. 3). Italy, Spain and Portugal reported vaccination coverage levels below the measured sero-immunity.

Discussion

This systematic review shows that, overall, seroprevalence for PV1 and PV3 is high in most countries and periods where data are available, although several birth cohorts showed sero-immunity gaps in specific populations. On average, Czech Republic, Italy, and Sweden showed immunity rates above 90% for almost all birth cohorts to all types of polio, while Belgium, Croatia, Greece, and the United Kingdom showed immunity rates below that threshold for almost all birth cohorts to all types of polio. On the other hand, the epidemiological evidence supported by good quality surveillance show, also in these countries, that general immunity levels have been sufficient to stop wild polioviruses circulation. France, Lithuania, The Netherlands and Spain showed some gaps over time in the immunization status of the
| Source | Country | Population | No. | Tier | P1 | P3 |
|--------|---------|------------|-----|------|----|----|
| Lamy (1978) | Belgium | Hospital and school | 218 | 85 | 14 | 67.3 |
| Parmakova (2011) | Bulgaria | General | 212 | 14 | 86.3 | 86.7 |
| Teply (1977) | Czech Republic | General | 212 | 77 | 80 | 83.5 |
| Malvy (1996) | France | General - Males | 212 | 97 | 95.4 | 94.3 |
| Malvy (1996) | France | General - Females | 212 | 97 | 95.4 | 94.3 |
| Diedrich (1995) | Germany | General | 212 | 89 | 88 | 84.4 |
| Diedrich (2007) | Germany | General population | 212 | 97 | 95.4 | 94.3 |
| Maass (1986) | Germany | Laboratory | 212 | 89 | 88 | 84.4 |
| Maass (1991) | Germany | Laboratory | 212 | 97 | 95.4 | 94.3 |
| Dalaina (1986) | Greece | General | 212 | 10 | 85 | 80.8 |
| Patti (2002) | Italy | General | 212 | 10 | 85 | 80.8 |
| Santoro (1984) | Italy | General | 212 | 10 | 85 | 80.8 |
| Mastroeni (1997) | Italy | Children | 212 | 10 | 85 | 80.8 |
| Volpi (1976) | Italy | General | 212 | 10 | 85 | 80.8 |
| Pianetti (1997) | Italy | Military personnel | 212 | 10 | 85 | 80.8 |
| Trivello (1994) | Italy | General | 212 | 10 | 85 | 80.8 |
| Natoli (1980) | Italy | High school | 212 | 10 | 85 | 80.8 |
| Veronesi (2013) | Italy | Obstetric department | 212 | 10 | 85 | 80.8 |

(Continued on next page)
Table 1. Studies included in the systematic review (n = 52) and estimated median P1 (%) and P3 (%) seroprevalence by decade of birth (Continued)

| Source                  | Country     | Population                      | No.  | Titer | 20s | 30s | 40s | 50s | 60s | 70s | 80s | 90s | 00s |
|-------------------------|-------------|---------------------------------|------|-------|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Tanzi (1991)            | Italy       | General                         | 1041 | 1:2   | 99.3| 98  | 99  | 97.6| 99  | 97.5| 99.9| 99.8| 99.3| 100 |
| Stagni (1979)           | Italy       | General                         | 1003 | 1:2   | 99  | 100| 99  | 100 | 99  | 100 | 99.9| 99.9| 99.9| 99.7|
| Riba (1995)             | Italy       | General                         | 816  | 1:2   | 91  | 101| 91  | 101 | 91  | 101 | 91.3| 91.3| 91.3| 91.3|
| Maiello (1995)          | Italy       | General                         | 934  | 1:2   | 96.7| 91.9| 94.6| 90.2| 94.3| 92.3| 96.6| 96.6| 97.9| 97.2|
| Andreassen (1994)       | Lithuania   | Pregnant                        | 100  | 1:4   | 91  | 91  | 91  | 91  | 91  | 91  | 91  | 91  | 91  | 91  |
| Andreassen (1994)       | Lithuania   | Policemen                       | 50   | 1:4   | 74  | 74  | 74  | 74  | 74  | 74  | 64  | 64  | 64  | 64  |
| Andreassen (1994)       | Lithuania   | Men at military camp            | 50   | 1:4   | 88  | 88  | 88  | 88  | 88  | 88  | 88  | 88  | 88  | 88  |
| Cohn-van Spaendonck (2001) | Netherlands | General                        | 7773 | 1:8   | 91.8| 84.6| 91.8| 84.6| 97.9| 90.2| 97.9| 90.2| 97.9| 90.2|
| Van der Maas (2014)     | Netherlands | General                        | 6386 | 1:8   | 88.6| 78  | 80  | 80.8| 81.7| 82.5| 91.5| 77.9| 94  | 80  |
| Cohn-van Spaendonck (2001) | Netherlands | Orthodox protestants refusing vaccination | 145 | 1:8   | 86.9| 61.3| 86.9| 61.3| 64  | 54.3| 64  | 54.3| 53.6| 54  |
| Van der Maas (2014)     | Netherlands | Orthodox protestants           | 480  | 1:8   | 80.3| 71.1| 80.3| 71.1| 71.1| 71.1| 71.1| 71.1| 71.1| 71.1|
| Português Ministério da Saúde (2004) | Portugal | General                        | 1133 | 1:8   | 90.1| 81.8| 90.1| 81.8| 81.8| 81.8| 81.8| 81.8| 81.8| 81.8|
| Pachon (2002)           | Spain       | General                         | 3615 | 1:2   | 95.7| 94.7| 95.4| 94.7| 95.4| 95.4| 95.2| 95.2| 95.2| 95.2|
| Plans Rubio (2006)      | Spain       | Primary school                  | 197  | 1:8   | 92  | 74.1| 94.5| 72.2| 92  | 74.1| 94.5| 72.2| 92  | 74.1|
| Bottiger (1972)         | Sweden      | General                         | 2291 | 1:4   | 93.6| 96.3| 91.3| 95.4| 94  | 94.9| 91.2| 95.2| 94.1| 96.4|
| Svensson (1998)         | Sweden      | General Female                  | 3390 | 1:4   | 96.8| 95.5| 98.9| 98.7| 98.5| 97.4| 98  | 96.1| 98  | 98  |
| Svensson (1998)         | Sweden      | General Male                    | 3390 | 1:4   | 93.7| 91  | 95.1| 93.7| 95.1| 91.9| 94.6| 92  | 96.1| 97.1| 98.5|
| White (1986)            | United Kingdom | General                        | 995  | 1:8   | 87  | 85.2| 81.2| 82.4| 86.6| 84.2| 91.6| 86.2| 89.1| 81.4|
| Cord (1979)             | United Kingdom | General                        | 1016 | 1:4   | 74.5| 59  | 74.9| 63.3| 73.8| 69.2| 67.7| 56.3| 64.7| 48.6|
| Roebeck (1982)          | United Kingdom | General                        | 919  | 1:8   | 79  | 78  | 85  | 80.4| 86  | 79.6| 84  | 78  | 76.9| 64.9|
| Mortimer (1975)         | United Kingdom | Children                     | 292  | 1:8   | 70  | 61  | 70  | 61  | 70  | 61  | 70  | 61  | 70  | 61  |
| Bainton (1979)          | United Kingdom | General                        | 293  | 1:8   | 95  | 89  | 95  | 89  | 95  | 89  | 95  | 89  | 95  | 89  |
| Joseph (1987)           | United Kingdom | University students             | 300  | 1:8   | 80  | 60  | 80  | 60  | 80  | 60  | 80  | 60  | 80  | 60  |
| Smith (1982)            | United Kingdom | Secondary schools              | 208  | 1:16  | 74  | 61.1| 74  | 61.1| 74  | 61.1| 74  | 61.1| 74  | 61.1|
| Galbraith (1969)        | United Kingdom | Children                     | 247  | 1:8   | 87  | 88  | 87  | 88  | 87  | 88  | 87  | 88  | 87  | 88  |
Data from Germany, Italy and the UK showed that there were considerable differences in immunity within the country. This difference was especially visible in Germany as former East-Germany showed immunity rates 20–30% lower than former West-Germany. In Italy differences could be partially explained by differences in implementing vaccination programmes as the regional health authorities are in charge of developing their own vaccination strategies.69

Relatively low immunity status was found in some countries for individuals born in the 60’s and 70’s. For the interpretation of these results, the different cut-offs used in the studies has to be considered. Additionally, vaccination programmes started at different points in time, with different vaccines and catch up strategies. Therefore it is very hard to assess the situation at the beginning of the polio vaccination campaigns. As an example, in some countries, like the former East-Germany, higher coverage levels were obtained only when IPV was replaced by OPV in the 60’s. Assuming these populations have not been exposed to the virus other than through vaccination, currently the seroprevalence would be below 80% for these individuals, aged 35 to 55 years, even without considering any waning immunity effect. Such evidence should not be considered as implying on immediate epidemic risk, given the generally high levels of sanitation and hygiene in the EU, but should be taken into consideration especially for individual protection of those in that age group traveling in areas where wild polioviruses are still circulating.

Reported vaccination coverage for 3 doses of polio for the last 30 years is generally very high. However, in countries where both reported coverage and seroprevalence data were available, these results were not always supported with equally high seroprevalence levels. This is the case for Bulgaria, Germany, and Greece. These differences could be due either to low potency of the vaccine used (primary vaccine failure) or to difficulties in vaccination coverage assessment in the countries, which would lead to inaccurate data reported to CISID. Vaccination coverage assessment is essential to monitor the performance of immunization systems in order to evaluate the progress toward the achievement of goals for controlling and/or eliminating vaccine preventable diseases. Last but not least, it is important to mention that a good overall coverage in a region or country does not guarantee the absence of transmission should polio virus be introduced. Areas or groups with low coverage can still exist. Being able to identify these groups would help implementing specific immunization campaigns.

This study presents some limitations. Many studies in the systematic review used cut off titres different from the ones recommended by WHO. Using cut off titres below 1:8 (22 studies) could lead to an overestimation of the population’s immunity to polio.
polio and, conversely, titres over 1:8 (6 studies) could lead to an underestimation of the population’s immunity. Considering this, the overall estimate of seroprevalence in this review is more likely to be biased toward overestimation of the EU population’s immunity. In addition, the current analysis did not take into consideration any decline of immunity over the time, since data are presented by birth cohort independently from when the seroprevalence was assessed. The sampling methods quality varied and was not optimal for some studies, so sampled subjects were not always representative of the country’s population.
Additionally, only 14 out of the 31 countries included in the EU/EEA are represented in the systematic review and as such the reported data may not represent the whole situation in the EU/EEA. On the other hand, these 14 countries account for around 80% of the EU/EEA population. Finally, no specific data on recognized vulnerable populations were reported in the studies, thus reported estimates are referred to the general population only.

**Conclusions**

The aim of the present review was to assess the immunological protection against WPV in the EU population, which is one of the components of the risk of WPV reintroduction in the European Region. Vaccine-derived polioviruses (VDVP) have not been taken into consideration and therefore PV1 and PV3 only have been presented as they are the only WPV circulating strains. Even though the immunity status of the EU/EEA population is high overall, this study points to some elements that could theoretically allow local transmission following introduction of poliovirus. In fact, immunological protection of EU/EEA population is patchy. Seroimmunity to polio was below the herd threshold in some countries, especially in relation to PV3. A gap in polio immunity in some EU/EEA countries for individuals currently aged 35 to 55 years was found. Additionally, discrepancies between vaccination coverage and seroprevalence levels in some countries are worth further investigation and clarification; reported immunization coverage in children and young adults may be overestimated in some countries, so leaving a higher number than might be assumed of susceptible in these young ages. Conversely it is important to underline that a population’s immunity is only one determinant of poliovirus
circulation in the community. Environmental factors and the overall hygiene level are crucial aspects for assessing the risk of polio re-introduction in the EU/EEA. The overall good levels of hygiene and sanitation in the EU/EEA countries represent an important risk mitigation factor. In conclusion, even in the presence of immunity gap, the overall protection of the EU/EEA population against the risk of wild polioviruses should be considered good.

**Recommendations**

Countries should make sure that their population is being vaccinated for polio to reduce the risk of poliovirus transmission in case of importation. Moreover, assessing immunity status should be priority for those traveling to areas where wild polioviruses are still circulating. One or more IPV booster doses, according to the national recommendations, should be considered in such cases. Increase in vaccination coverage should go hand to hand with proper vaccination monitoring. For some countries no seroprevalence studies were available (or not recent ones), therefore further research would be advised to get a better overview of the EU/EEA situation. Monitoring of hard to reach populations is also needed in order to assess the susceptibility of polio in these groups. Finally, it would be advised to comply with the WHO guidelines to enable more accurate comparison between studies.

**Disclosure of Potential Conflicts of Interest**

No potential conflicts of interest were disclosed.

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