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Review

A report on the status of vaccination in Europe

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ABSTRACT

Vaccine policy, decision processes and outcomes vary widely across Europe. The objective was to map these factors across 16 European countries by assessing (A) national vaccination strategy and implementation, (B) attributes of healthcare vaccination systems, and (C) outcomes of universal mass vaccination (UMV) as a measure of how successful the vaccination policy is.

A. Eleven countries use standardised assessment frameworks to inform vaccine recommendations. Only Sweden horizon scans new technologies, uses standard assessments, systematic literature and health economic reviews, and publishes its decision rationale. Time from European marketing authorisation to UMV implementation varies despite these standard frameworks. Paediatric UMV recommendations (generally government-funded) are relatively comparable, however only influenza vaccine is widely recommended for adults.
B. Fourteen countries aim to report annually on national vaccine coverage rates (VCRs), as well as have target VCRs per vaccine across different age groups. Ten countries use either electronic immunisation records or a centralised registry for childhood vaccinations, and seven for other age group vaccinations.
C. National VCRs for infant (primary diphtheria tetanus pertussis (DTP)), adolescent (human papillomavirus (HPV)) and older adult (seasonal influenza) UMV programmes found ranges of: 89.1% to 98.2% for DTP-containing vaccines, 5% to 85.9% for HPV vaccination, and 4.3% to 71.6% for influenza vaccine. Regarding reported disease incidence, a wide range was found across countries for measles, mumps and rubella (in children), and hepatitis B and invasive pneumococcal disease (in all ages).

Abbreviations: BCG, Bacillus Calmette-Guerin; CR, centralised registry; DTP, diphtheria tetanus pertussis; ECDC, European Centre for Disease Prevention and Control; EIR, electronic immunisation record; EMA, European Medicines Agency; EU, European Union; HPV, human papillomavirus; IPD, invasive pneumococcal disease; HTA, health technology assessment; IPD, invasive pneumococcal disease; KPI, key performance indicator; Men, meningitis; MMR, measles, mumps, rubella; NITAG, National Immunization Technical Advisory Groups; OOP, out-of-pocket; QIV, quadrivalent influenza vaccine; TIV, trivalent influenza vaccine; UK, United Kingdom; UMV, universal mass vaccination; VCR, vaccination coverage rate; WHO, World Health Organization.

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These findings reflect an individual approach to vaccination by country. High VCRs can be achieved, particularly for paediatric vaccinations, despite different approaches, targets and reporting systems; these are not replicated in vaccines for other age groups in the same country. Additional measures to improve VCRs across all age groups are needed and could benefit from greater harmonisation in target setting, vaccination data collection and sharing across EU countries.

Contents

1. Introduction

Although national immunisation strategies have traditionally focussed on infants and children, policymakers increasingly seek to protect the wider population against infectious diseases by moving towards a life-course immunisation approach [1]. At the same time, there is greater public interest and debate about the role of immunisation and the safety and regulation of vaccines [2]. Financial and social pressures on healthcare systems in Europe have also contributed to the increased adoption of evidence-based evaluation of vaccines in order to maximise their benefits in a given population [3]. Decision-making for vaccination policy varies widely, with different processes and outcomes in each country. Countries need to improve their immunisation strategies using evidence-based, transparent and sustainable processes [2,3]. Recommendations and vaccination policies are different across European countries, as decision-making remains country-specific [4] reflecting varying epidemiology as well as country-specific differences in healthcare systems, level of evidence, vaccine acceptability and financing [3]. The World Health Organization (WHO) Regional Office for Europe (WHO-Europe) defined priority areas for action, as well as indicators and targets for vaccination, in order to meet its vision of all countries being able to provide equitable access to high-quality, safe, affordable vaccines and immunization services throughout the life course in its European Vaccine Action Plan (EVAP) 2015–2020 [5]. Additionally the EU now believes that vaccination programmes are increasingly fragile; in the face of low uptake of vaccines, vaccine hesitancy, the increasing cost of new vaccines and shortages in vaccine production and supply in Europe.

The objective of this research was to map the status of vaccination across Europe by considering together the national vaccination strategy, attributes of healthcare systems and the vaccine coverage rate (VCR), and assessing the outcomes of universal mass vaccination (UMV) using the VCR.

2. Methods

Countries use multidisciplinary groups of independent national experts (National Immunization Technical Advisory Groups, NITAGs) to assess evidence and advise their governments on immunisation policies (e.g., both on choice of new vaccines and adjustments required to existing strategies and schedules). A healthcare systems approach was applied to examine the relationship between NITAG decision-making, attributes of the healthcare system (where the NITAGs may or may not have an influence), and outcomes of the UMV (i.e., using VCR) (Fig. 1). Research questions, to address each point in Fig. 1, were formulated to assess whether and how different aspects of vaccination policy (NITAG decision-making, monitoring and surveillance) impact on UMV.

A total of 16 European countries (i.e., Austria, Belgium, Bulgaria, Croatia, Finland, France, Germany, Greece, Italy, the Netherlands, Poland, Romania, Spain, Sweden and the United Kingdom (UK), in the EU, and Switzerland) were included. This was for the increased feasibility of working with a limited number of countries and being able to conduct the research in a timely fashion. Countries included were predominantly the most populous European countries with a mixture of payment models (e.g., vaccines provided via individual prescriptions reimbursed by insurance or with a co-payment, or, purchased through government tenders and essentially free of charge to the patient).

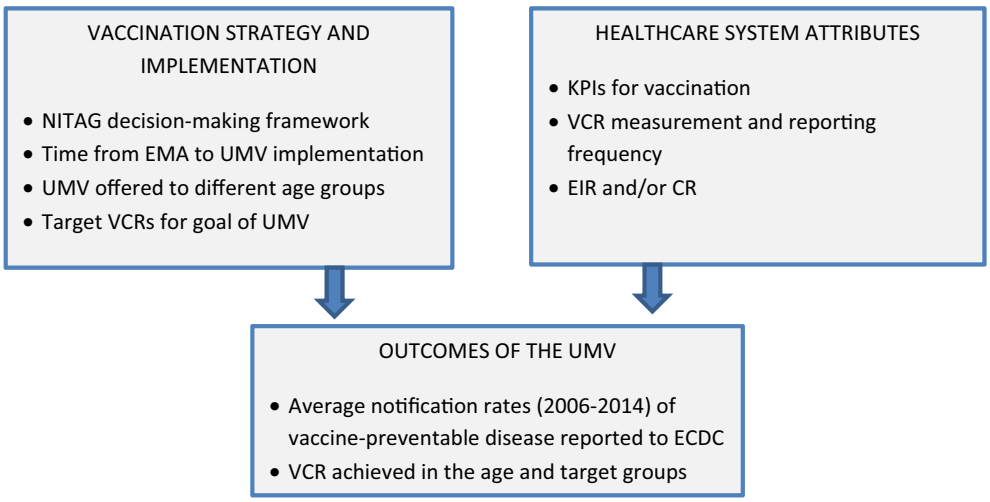

Fig. 1. Overview of health systems approach. CR: centralised registry; ECDC: European Centre for Disease Prevention and Control; EIR: electronic immunisation record; EMA: European Medicines Agency; KPI: key performance indicator; NITAG: National Immunization Technical Advisory Group; UMV: universal mass vaccination; VCR: vaccine coverage rate.

Data were collected through secondary research and verified through interviews with country experts experienced in vaccine-related research and policy. The most recent publicly available data were used. Searches were conducted on publicly available information sources in the native language, including official government and supranational websites, peer-reviewed publications on vaccine policy and conference abstracts. Search terms reflected key terminology used to formulate policy briefs, reports, and regulations. Search terms as well as country-specific information were translated where necessary. The research questions were refined following an advisory panel of a subset of experts from Germany, France, Italy, Switzerland, the Netherlands and the UK. Findings were compiled in a data repository (MS Excel) and information was coded and streamlined to ensure consistent use of key terminology.

Time intervals were retrieved for the first vaccine brand to be included in national UMVs for a given disease (i.e., rotavirus, human papillomavirus (HPV), paediatric and adult pneumococcal and seasonal influenza vaccines, meningococcal B and herpes zoster vaccines). This provided an overview across a range of age groups, to estimate the length of time each country takes from European Medicines Agency (EMA) approval, which is common to all countries except Switzerland in our analysis, to NITAG recommendation and to UMV implementation.

The reimbursement status of recommended (including mandatory) vaccines was reviewed and classified as: fully reimbursed, subject to co-payment or paid out-of-pocket (OOP). Data were broadly divided by age and antigen into paediatric vaccination (from birth to 18 years) and adult vaccination (pregnant women, adult boosters and vaccines for older adults i.e., usually considered to be over 65 years). Data on risk groups other than pregnant women were not included.

Public information sources were searched to find whether countries set strategic goals and targets for vaccination, the last time the goal was set, how often it was reported and the information systems underlying VCR reports (electronic immunisation records (EIRs) and centralised registries (CRs)).

The notification rates for each country, as reported to the European Centre for Disease Prevention and Control (ECDC) between 2006 and 2014, were retrieved to calculate the average notification rate of measles, mumps and rubella (MMR), hepatitis B and invasive pneumococcal disease (IPD), per country by age group.

The VCR for the primary infant series of diphtheria tetanus pertussis (DTP) vaccination was reviewed and compared across countries as these antigens are established across all countries in scope, and this is part of EVAP goal 4 [5]. Childhood booster vaccinations of DTP-containing vaccines, however, were excluded as schedules vary widely. Similarly, the VCR for HPV vaccination (complete course) in adolescents, and for seasonal influenza in older adults was reviewed and compared as these vaccines are also common across most countries.

3. Results

3.1. Vaccination strategy and implementation

3.1.1. How do NITAGs make recommendations on new UMVs?

In some countries NITAGs are independent from health technology assessment (HTA) bodies, while others are part of the HTA body which usually has a role in assessing pharmaceuticals and devices for potential use in that country. From publicly available information across the 16 countries, NITAG decision-making includes horizon scanning for new products in seven countries, of which only France and the UK specify performing horizon scanning for vaccines. A systematic framework or standard operating procedure for vaccine assessment is applied in 11 countries; 10 conduct a systematic literature review, 11 conduct an economic evaluation, and eight countries do both. Ten countries publish their rationale for the positive or negative decision made regarding inclusion of the vaccine in the UMV. Only Sweden currently applies all of these stages to a systematic vaccine assessment (Table 1). Romania had a NITAG in 2015, which was subsequently disbanded.

3.1.2. What is the time period from vaccine marketing authorisation to UMV implementation?

The range for EMA authorisation to NITAG recommendation was considerably greater than the range from NITAG recommendation to UMV implementation. The time of NITAG recommendation, however, was not known for all vaccines and in all countries, so the average time from EMA approval to UMV implementation is presented (Table 2), calculated from the date of the first EMA approval of a vaccine for a disease (i.e., in the case of multiple vaccines approved for one disease) until the UMV implementation date. As some countries are still deciding on implementation, the average times provided are underestimates. For full details by country, see Appendix Table 2.

Table 1
Country approaches to systematic assessment.

	Countries that apply this approach	Countries that do not apply this approach
Existence of NITAG (self-designated)	Austria, Belgium, Croatia, Finland, France, Germany, Greece, Italy, Netherlands, Poland, Romania Spain, Switzerland, UK	Bulgaria, Sweden
Horizon scanning (*specified for vaccines)	*France,*UK, Italy, Netherlands (from Dec 2017), Spain, Sweden	Austria, Belgium, Bulgaria, Croatia, Finland, Germany, Greece, Poland, Romania, Switzerland
Systematic framework or standard procedures	Austria, Croatia, Finland, Germany, Italy, Netherlands, Poland, Spain, Sweden, Switzerland, UK	Belgium, Bulgaria, France, Greece, Romania
Systematic literature review	Austria, Croatia, Finland, Germany, Greece, Italy, Netherlands, Poland, Sweden, Switzerland	Belgium, Bulgaria, France, Spain, Romania, UK
Recommendation process includes consideration of results from health economic evaluation (†not mandatory)	Austria, Finland, France, †Germany, Italy, Netherlands, Poland, Spain, Sweden, Switzerland, UK	Belgium, Bulgaria, Croatia, Greece, Romania
Rationale published	Austria, Belgium, Finland, France, Germany, Netherlands, Spain, Sweden, Switzerland, UK	Bulgaria, Croatia, Greece, Italy, Poland, Romania

Sources: general [6] & by country: Austria [7], Belgium [8], Bulgaria [9], Croatia [10], Finland [11], France [12,13], Germany, Greece [14], Italy [15], Netherlands [16], Poland [17], Romania [18], Spain [19], Sweden [20], Switzerland [21], UK [22,23].

Table 2
Average time from first authorisation for disease to UMV implementation.

Vaccine	Number of UMV countries	Average time (range)
Rotavirus vaccine	9 (Austria [24], Belgium [25,26], Bulgaria [27], Finland [28], Germany [29,30], Greece [31,32], Italy [33], Poland [34], UK [28])	65 months (11 months Belgium, 135 months Italy)
HPV vaccine	15 (Austria [35], Belgium [36,37], Bulgaria [38], Croatia [39], Finland [40], France [41–43], Germany [44–46], Greece [47], Italy [48,49], Netherlands [50–52], Poland [53,54], Spain [55], Sweden [56,57], Switzerland [58], UK [59,60])	36 months (5 months Spain, 117 months Croatia)
Paediatric pneumococcal vaccine	13 (Austria [61], Belgium [61,62], Bulgaria [63], Finland [64,65], France [61,66], Germany [61,67], Greece [61], Italy [68,69], Netherlands [61,70], Spain [61,71,72], Sweden [61,73,74], Switzerland [61,75], UK [61,76])	55 months (13 months Bulgaria, 100 months Sweden)
Paediatric influenza vaccine	2 (Finland [77] and UK [78])	Not applicable given yearly update of the vaccine. UMV first in Finland for seasonal TIV in 2007* and the UK in 2014.
Meningococcal B vaccine	2 (UK [79,80] and Italy [33])	36 months (32 months UK, 40 months Italy)
Adult pneumococcal vaccine	5 (Belgium [81–83], Germany [84], Greece [85], Italy [86] and UK [76,82,87,88])	158 months (67 months Greece, 217 months Germany)
Herpes zoster vaccine	3 (France [89,90], Italy [33], UK [91,92])	114 months (88 months UK, 133 months Italy)

HPV: human papillomavirus; TIV: trivalent influenza vaccine; QIV: quadrivalent influenza vaccine; UK: United Kingdom; UMV: universal mass vaccination.
* TIV for children was subsequently changed to QIV when this vaccine became available. The remaining 14 countries in our analysis do not offer paediatric seasonal influenza vaccine as part of the UMV.

3.1.3. Current UMV strategies and programmes

3.1.3.1. Childhood and adolescent UMV vaccination (from birth to 18 years of age). In general, recommended vaccines (which includes mandatory vaccines) in this age group are funded by the government or third-party payers. In France, the majority of recommended vaccines are available with a co-payment through private insurance, and in Austria, Poland and Romania, some recommended vaccines are available for private purchase (OOP). It should be noted that countries vary in attitudes and ability to access OOP vaccines; for example, this is relatively unusual in the Netherlands and Sweden yet more common in e.g., Spain, Austria, Greece and Romania. Vaccines that are not generally recommended for UMV in this age group for the cohort countries include Bacillus Calmette-Guerin (BCG), hepatitis A, varicella, Meningitis (Men) B, MenACWY, influenza and to some extent MenC and rotavirus, however, these may be available for private purchase and are generally funded for at-risk groups. Full details about vaccines recommended in the UMV programme, with levels of funding, can be found in Fig. 2 by country.

3.1.3.2. Non-paediatric UMV vaccination. Recommendations and levels of funding for the UMV vaccines assessed can be found in Fig. 3 by country, for pregnant women, adults and older adults.

3.1.3.2.1. Pregnant women vaccination. UMV vaccines recommended for pregnant women are influenza and diphtheria, tetanus and pertussis. Recommendations and funding arrangements vary between cohort countries. Influenza vaccination is recommended in all countries except Bulgaria and the Netherlands. Diphtheria, tetanus and pertussis vaccination is recommended and fully funded in Belgium, Greece, Italy, Spain, Switzerland and the UK.

3.1.3.2.2. Adult vaccination. Adult UMV vaccinations include diphtheria, tetanus, pertussis and hepatitis B (only recommended in Poland for OOP purchase). Diphtheria, tetanus and pertussis are recommended in all countries except Croatia, the Netherlands, Romania and the UK, with full funding in most of these countries.

3.1.3.2.3. Older adult (usually considered to be ≥65 years of age) vaccination. Influenza, zoster, pneumococcal, diphtheria, tetanus and pertussis are UMV vaccines for older adults. All are recommended for UMV in Austria (through OOP financing) and are fully funded in Greece and Italy. In Germany, herpes zoster vaccination is not recommended at the national level but in single federal states (e.g., in Saxony).

3.1.4. What are the goals of the UMV?

Vaccination goals to monitor specific vaccine performance were identified in all countries except Bulgaria, Finland and Poland and

UMV[28]	AT	BE	BG	HR	FI	FR	DE	GR	IT	NL	PL	RO	SP	SE	CH	UK
BCG	✖	✖	✓	✓	✖	✖	✖	✖	✖	✖	✓	✓	✖	✖	✖	✖
Hepatitis B	✓	✓	✓	✓	✖	✓	✓	✓	✓	✓	✓	✓	✓	✖	✓	✓
Polio	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Diphtheria	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Tetanus	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Pertussis	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Hib	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Pneumococcal	✓	✓	✓	✖	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Rotavirus	✓	✓	✓	✖	✓	✖	✓	✓	✓	✖	✓	✖	✖	✖	✖	✓
Measles	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Mumps	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Rubella	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Hepatitis A	✖	✖	✓	✖	✖	✖	✖	✓	✖	✖	✓	✖	✖	✖	✖	✖
Varicella	✓	✖	✖	✖	✓	✖	✓	✓	✓	✖	✖	✖	✓	✖	✓	✖
HPV	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✖	✓	✓	✓	✓
MenC	✓	✓	✓	✖	✖	✓	✓	✓	✓	✓	✓	✖	✓	✖	✓	✓
MenACWY	✓	✖	✓	✖	✖	✖	✖	✓	✓	✖	✓	✖	✖	✖	✖	✓
MenB	✓	✖	✖	✖	✖	✖	✖	✖	✓	✖	✓	✖	✖	✖	✖§	✓
Influenza	✓	✖	✖	✖	✓	✓	✖	✖	✖	✖	✓	✖	✖	✖	✖	✓
Legend	✓ Recommended for UMV								✖ Not recommended for UMV							
		Funded/reimbursed					Out-of-pocket (OOP)					Co-payment				
Abbreviations	AT: Austria, BE: Belgium, BG: Bulgaria, HR: Croatia, FI: Finland, FR: France, DE: Germany, GR: Greece, IT: Italy, NL: Netherlands, PL: Poland, RO: Romania; SP: Spain, SE: Sweden, CH: Switzerland**§ (not licensed)**, UK: United Kingdom; BCG: Bacillus Calmette–Guérin; Hib: Haemophilus influenzae B; HPV: human papillomavirus; Men: meningitis; UMV: universal mass vaccination.															

Fig. 2. Recommended childhood and adolescent UMV vaccines by country and funding level (2017).

included target VCRs for both seasonal influenza vaccination and MMR vaccination in six countries (Table 3). In addition to measles and influenza, some countries also set specific target national VCRs for other vaccines. Belgium and the UK had key performance indicators (KPIs) for paediatric vaccination: i.e., 80% VCR target for infants and toddlers under 18 months old in Belgium, and 95% VCR target for children under four years old in the UK.

3.2. Healthcare system attributes

3.2.1. Vaccination KPIs, VCR frequency and reporting system

Countries typically had vaccine-specific KPIs (e.g. a target VCR) across all age groups. Table 3 shows that 14 countries report VCRs at a national level for several vaccines across all age groups, with 13 of these stating they report these data yearly, however, these data were not always publicly available each year. The UK reports VCRs on both a quarterly and yearly basis for most vaccines. No publicly available national level data on the frequency of VCR reporting in Austria and Belgium were identified. The publication of the latest reported data is in Table 3, however, this may not always reflect the data collection date. For example, in Germany, data on older adults for pneumococcal vaccination were based on a 2008–2011 survey (published in 2013) and for seasonal influenza, the last report was from the 2015–2016 season (published in 2017). In Germany, VCR based on school entry examinations are published yearly, while VCR from claims data are not published for all vaccines every year.

In terms of the information systems underlying VCR reporting, a distinction was made between an EIR and a CR which held only national level data. The use of national health data surveys was not considered an appropriate proxy for a centralised registry. Ten countries had either a CR or EIR for reporting childhood vaccinations, and seven had either a CR or EIR for other age group vaccinations. Not all regions in Italy have an EIR system, some still send paper copies to a CR. Germany has not established a comprehensive standardised system for VCR data collection but uses regular sources typically from specific surveys, school entry data or claims data. Full details are provided in the Appendix.

3.3. Outcomes of the UMV

3.3.1. Reported average disease notification rates for vaccine-preventable disease

The third and final component to the research was to assess UMV outcomes, using the latest data on the reported incidence of vaccine-preventable disease, and the VCR achieved in paediatric and adult populations.

The average notification rates for each country were based on data reported to the ECDC from 2006 to 2014 for measles, mumps and rubella [142], and from 2010 to 2014 for hepatitis B [143] and IPD [142]. Figs. 4 and 5 present the country data for measles, mumps and rubella in children and hepatitis B in all age groups, and for IPD in infants, children and older adults (available for 12 countries), respectively. In both adults and children, there is a wide

	AT	BE	BG	HR	FI	FR	DE	GR	IT	NL	PL	RO	SP	SE	CH	UK
UMV for Pregnant Women[28]																
Diphtheria	✗	✓	✗	✗	✗	✗	✗	✓	✓	✗	✓	✓	✓	✗	✓	✓
Tetanus	✗	✓	✗	✗	✗	✗	✗	✓	✓	✗	✓	✓	✓	✗	✓	✓
Pertussis	✓	✓	✗	✗	✗	✗	✗	✓	✓	✓	✓	✓	✓	✗	✓	✓
Influenza	✓	✓	✗	✓	✓	✓	✓	✓	✓	✗	✓	✓	✓	✓	✓	✓
UMV for Adults[28]																
Diphtheria	✓	✓	✓	✗	✓	✓	✓	✓	✓	✗	✓	✗	✓	✓	✓	✗
Tetanus	✓	✓	✓	✗	✓	✓	✓	✓	✓	✗	✓	✗	✓	✓	✓	✗
Pertussis	✓	✓	✓	✗	✓	✓	✓	✓	✓	✗	✓	✗	✓	✓	✓	✗
Hepatitis B	✗	✗	✗	✗	✗	✗	✗	✗	✗	✗	✓	✗	✗	✗	✗	✗
UMV for Older adults (≥60 or 65 years of age)[28]																
Zoster	✓	✗	✗	✗	✗	✓	✗	✓	✓	✗	✗	✗	✗	✗	✗	✓
Pneumococcal	✓	✓	✓	✗	✓	✗	✓	✓	✓	✗	✓	✗	✗	✗	✗	✓
Diphtheria	✓	✓	✓	✗	✓	✓	✓	✓	✓	✗	✓	✗	✓	✓	✓	✗
Tetanus	✓	✓	✓	✓	✓	✓	✓	✓	✓	✗	✓	✗	✓	✓	✓	✗
Pertussis	✓	✓	✓	✓	✓	✗	✓	✓	✓	✗	✓	✗	✗	✓	✓	✗
Influenza	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Legend	✓ Recommended for UMV					✗ Not recommended for UMV										
	Funded/reimbursed					Out-of-pocket (OOP)						Co-payment				
Abbreviations	AT: Austria, BE: Belgium, BG: Bulgaria, HR: Croatia, FI: Finland, FR: France, DE: Germany, GR: Greece, IT: Italy, NL: Netherlands, PL: Poland, RO: Romania, SP: Spain, SE: Sweden, CH: Switzerland, UK: United Kingdom; UMV: universal mass vaccination.															

Fig. 3. Recommended vaccines by country and funding level for pregnant women, adults and older adults (2017).

range in reported disease incidence particularly for hepatitis B and rubella. Where data were reported, the incidence per 100,000 ranged from 0.13 (France) to 16.55 cases (Sweden) for hepatitis B, and from 0.02 (Netherlands) to 24.10 cases (Poland) for rubella.

Belgium, France, Germany and Switzerland did not report notification rates for IPD (no systematic surveillance) in the time frame reviewed; Bulgaria and Croatia reported very low numbers, no rates for infants or older adults were reported for Croatia, and no data reported before 2012. Fig. 5 shows higher IPD notification rates in the older adult population versus young children, which could be explained by only 9 of the 16 cohort countries recommending pneumococcal vaccination in this age group, an ageing population, and, low vaccine coverage and effectiveness.

3.3.2. What is the vaccine coverage rate (VCR) in the target populations?

Table 4 shows the national level data on VCR from the most recent published figures for an infant, adolescent and older adult UMV programme (i.e., DTP, HPV and seasonal influenza programmes, respectively). There were differences in the level of publicly available information.

For the primary DTP-containing series in all 16 countries, the primary VCR ranged from 89.1% (Romania) to 98.2% (Finland and Sweden). Where possible, the range of VCR was retrieved to highlight regional variations as one of the limitations of this analysis is the focus on national level data.

All of the countries in scope offer HPV vaccination in their UMV programme except Romania [144] which discontinued its HPV UMV programme. Vaccine coverage rates were not available for Austria and Croatia, and ranged from 14.1% in Bulgaria to 85.9% in the UK.

In the case of seasonal influenza, VCRs were available for 14 countries (with the exception of Bulgaria and Switzerland). These ranged from 4.3% (Poland) to 71.6% (UK). The ranges retrieved showed a maximum of 74.5% in some parts of the UK.

4. Discussion

The organisation, funding and delivery of healthcare is the responsibility of individual countries in Europe. The findings clearly reflect this individual approach to vaccination: no single country stood out as a best practice model of vaccination and public health control of infectious diseases. In some countries, VCRs were high, particularly for the primary vaccination series, despite having different NITAG assessment approaches, KPIs and underlying information systems. Both a programmatic (i.e., highly centralised decision-making and implementation supported and coordinated by national or regional level public health) and a decentralised (following NITAG decision, individual prescribers implement vaccination policy) approach produced high VCRs.

There was considerable variation between country schedules, with only two vaccines for which KPIs were widely applied – influenza and MMR. This is despite the adoption of the EVAP action plan by European Union member states, which explicitly identified as goals sustaining polio-free status, elimination of measles and rubella, control of hepatitis B infection and, meeting 95% coverage of three doses of DTP-containing vaccines. Italy was notable for setting KPI targets for many paediatric vaccines in its UMV, and for herpes zoster vaccine for older adults since 2017. Influenza was the only non-paediatric UMV vaccine with a KPI, however, this is confounded by variations in VCR ranging from 4.3% in Poland to 71.6% in the UK. Europe has a growing ageing population with

Table 3
Vaccine-specific KPIs, and frequency of VCR reporting.

Country	Vaccine-specific KPIs by target group				Frequency of VCR reporting				Child-hood		Other age	
	Vaccine	Target group	Target VCR (%)	Target established	Vaccine	Target Group	Report frequency	Last report	EIR	CR	EIR	CR
Austria [93–96]	MMR	Children	95	2015	NR	_	_	_	No	No	No	No
	Influenza	Older adults, underlying condition	75	2010								
Belgium [95–98]	MMR	Children	95	2015	NR	_	_	_	Yes	No	Yes	No
	Influenza	Pregnant, Risk group < 65y	50	2015								
		Older adults	75	2015								
		HCP	80	2015								
	Pertussis	HCP	80	2015								
Bulgaria [99]	NR	_	_	_	Polio, DTP, BCG, HepB, Hib, MMR, Pneumococcal, Rotavirus gastroenteritis, HPV	Infant, Toddler, Adolescent	Yearly	2016	No	No	No	No
Croatia [100,101]	MMR	Children	95	2007	BCG, HepB, Polio, DTP, Hib, MMR	Infant, Toddler, Adolescent	Yearly	2015	NR	NR	NR	NR
					DT	Older adults	Yearly	2015				
Finland [102–105]	NR	_	_	_	Polio, DTP, Hib, Pneumococcal, Rotavirus, MMR, HepA, HPV	Infant, Toddler, Adolescent	Yearly	2016	Yes	Yes	Yes	Yes
					Influenza	Older adults	Yearly	2017				
France [106–108]	MMR	Children	80–95	2005	DTP, MMR, Pneumococcal		Yearly	2015	Yes	Yes	No	No
					HepB, Polio, Hib	Infant, Toddler, Adolescent	Yearly	2015				
					HPV, Meningococcal		Yearly	2016				
	Influenza	Risk groups	95*		Influenza	Older adults	Yearly	2016				
Germany [109–113]	MMR	Children	95	2015	HepB, Polio, DTP, Hib, Varicella, Pneumococcal, MMR, Meningococcal	Infant, Toddler, Adolescent	Yearly	2017	No	No	No	No
					HPV		Yearly	2017				
					Pneumococcal, Influenza	Older adults		2013, 2017				
Greece [96,114,115]	MMR	Children	95*		BCG, HepB, Polio, DTP, Hib, Pneumococcal, Rotavirus, MMR, HepA, Varicella, Meningococcal, Influenza	Infant, Toddler, Adolescent		2013	No	No	No	No
Italy [33,95,96,116,117]	MMR	Children	95	2017	HepB, Polio, DTP, Hib, HPV, Pneumococcal, MMR, Varicella, Meningococcal	Infant, Toddler, Adolescent	Yearly	2015	Yes	No	Yes	No
	Varicella		95	2017								
	DTP	Infant, Children	90–95	2017								
	IPV		95	2017								
	Hepatitis B	Infant	95	2017								
	Pneumococcal		95	2017								
	HPV	Adolescent	95	2017								
	Meningococcal	Infant, Adolescent	95	2017								
	Hib		95	2017								
	Influenza	Older adults, Risk groups	75–95	2017	Influenza	Older adults	Yearly	2015				
	Zoster	Older adults	50 (by 2019)	2017								
	Pneumococcal		75 (by 2019)	2017								
Netherlands [96,118,119]					HepB, Polio, DTP, Hib, MMR, HPV Pneumococcal, Meningococcal	Infant, Toddler, Adolescent	Yearly	2016	Yes	Yes	Yes	No
	Influenza*	Elderly, risk groups			Influenza	Older adults, risk groups	Yearly	2015				
Poland [120,121]	NR	_	_	_	BCG, HepB, Polio, Influenza Pneumococcal, Varicella, HPV	Infant, Toddler, Adolescent		2015	No	No	No	No
					DTP, Hib, MMR		Yearly	2015				
					Influenza	Older adults		2015				

(*continued on next page*)

Table 3 (*continued*)

Country	Vaccine-specific KPIs by target group				Frequency of VCR reporting				Child-hood		Other age	
	Vaccine	Target group	Target VCR (%)	Target established	Vaccine	Target Group	Report frequency	Last report	EIR	CR	EIR	CR
Romania [33,95,96,122–124]	MMR	Children	94–98	2010	MMR	Infants, Toddlers	Yearly	2015	Yes	Yes	No	No
Spain [95,96,125,126]	MMR	Children			HepB, Polio, DTP, Hib, MMR, HPV, Meningococcal	Infant, Toddler, Adolescent	Yearly	2015	Yes	No	Yes	No
	Influenza	Older adults	65*		Influenza	Older adults	Yearly	2016				
Sweden [73,95,127–129]	MMR	Children	95	2015	BCG, HepB, Polio, DTP, Hib, Pneumococcal, MMR	Infant, Toddler, Adolescent	Yearly	2014	Yes	Yes	Yes	No
					Influenza	Older adults	Yearly	2015				
Switzerland [130–132]	MMR	Children	95	2011	HepB, Polio, DTP, Hib, HPV, Pneumococcal, MMR, HepA, Meningococcal	Infant, Toddler, Adolescent	Yearly	2016	Yes	No	Yes	No
UK [95,96,133–141]	MMR	Children	95	2015	Polio, DTP, Hib, Pneumococcal,	Infant, Toddler,	Quarterly,	2016	Yes	No	No	No
	Influenza	Underlying condition	55	2016	Rotavirus, MMR, Meningococcal,	Adolescent	Yearly					
		Older adults, HCP	75	2016	Influenza							
		Children	40–65	2016								
	Zoster	Older adults	100	2017	HPV		Yearly	2016				
	Pneumococcal		100	2016	Influenza	Pregnant	Quarterly,	2015				
						Older adults	Yearly	2016				

* Expert opinion; CR: centralised registry; DTP: diphtheria, tetanus, pertussis; EIR: electronic immunisation record; HCP: healthcare professional; Hep: hepatitis; Hib: Haemophilus influenzae B; HPV: human papillomavirus; IPV: inactivated polio vaccine; KPI: Key performance indicator; MMR: measles mumps, rubella; NR: Not reported; VCR: vaccine coverage rate.

potentially higher morbidity due to infectious disease, therefore widespread vaccination could significantly reduce the healthcare burden in older adults. Coverage in this age group, however, remains low as; comprehensive national policies for vaccination of older adults are lacking, many general practitioners do not recommend or prioritise vaccination of older adults, cost barriers exist and result in inequitable coverage and, older adults and healthcare professionals lack understanding of the benefits of vaccination [170]. Similar factors were reported to affect vaccination coverage in adults (i.e., lack of knowledge among adults and healthcare professionals of vaccine recommendations and benefits in adults as well as lack of funding or cost concerns) [171]. Key factors to improve VCR among adolescents include educating adolescents and addressing who has responsibility for delivering vaccines [172]. These barriers to life course vaccination are recognized in Europe and reflected in EVAP objective 3 which highlights the need to research, develop and implement the best targeted approaches to vaccinate underserved populations such as adolescents and adults [5].

Regardless of individual differences, VCRs in different age groups were reported across all countries and were used to assess UMV outcomes. Data on incidence rates reported to ECDC were also captured to determine the extent of control of vaccine-preventable diseases, however, these data are likely to be confounded by the surveillance programme strength and reporting accuracy. For seasonal influenza, the data show a clear disparity in VCRs achieved; 10 countries either do not report VCRs (Bulgaria and Switzerland) or have a VCR below 50% (Austria, Croatia, Finland, France, Germany, Greece, Poland and Romania), despite the 2009 EU commitment [173] to reach the WHO-agreed goal of 75% VCR in older adults preferably by the 2014–15 winter season. Only Belgium, Italy, the Netherlands, Spain, Sweden and the UK achieve a 50% or greater VCR.

Overall, the data on VCRs and KPIs explicitly show the continued focus and likely prioritisation of paediatric immunisation, and are not indicative of a trend towards the stated goal of a life-course vaccination approach [1] that prioritises infectious disease control in all ages. It appears a missed opportunity for countries to not set these KPIs despite making the investment in public health for non-paediatric age groups. Italy and the UK are notable exceptions, as they track seasonal influenza, zoster and pneumococcal vaccination in older adults.

Despite KPI targets for VCRs exceeding 90% in most countries, the reported rate of measles, rubella and mumps is much higher in the 16 countries included than for any other vaccine-preventable disease dataset held by the ECDC both in adults and children, demonstrating the wider impact of reduced MMR coverage. The research did not assess recent legislative initiatives that mandate vaccination; such as the introduction in Germany of mandatory healthcare professional consultations on vaccines (pre-school or kindergarten) in 2015 [174], the decision of Italy to make 10 paediatric vaccinations mandatory in 2017 [175], and decisions in France concerning 11 paediatric vaccinations from 2018 [176]. These initiatives aim to increase VCRs, where vaccine scepticism and hesitancy may have contributed to lower than expected coverage. This follows the perceived success of mandates in the USA and Australia, which may have a potentially beneficial public health impact, although they could be contentious with the public.

This study shows a wide range in the length of time from marketing authorisation at a European level to NITAG decision and then to UMV implementation. In general, however, time to population use from EMA authorisation was faster for paediatric vaccines in this analysis than for vaccines in older adults (pneumococcal and herpes zoster vaccination). NITAGs may wish to consider if they assess the needs of their (older) adult populations in the same way as their paediatric population.

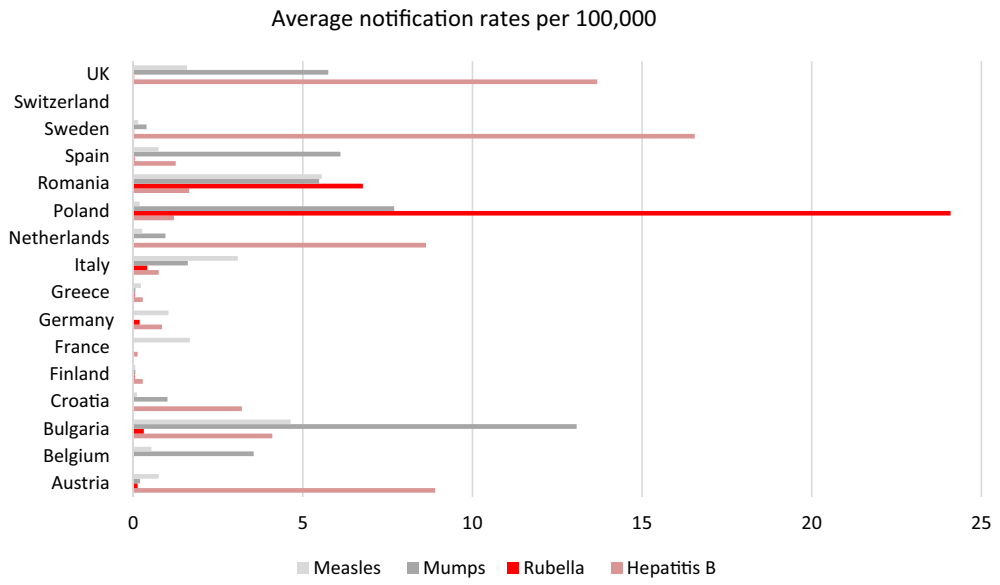

Fig. 4. Average notification rates of measles, mumps, rubella (children) and hepatitis B (all ages).

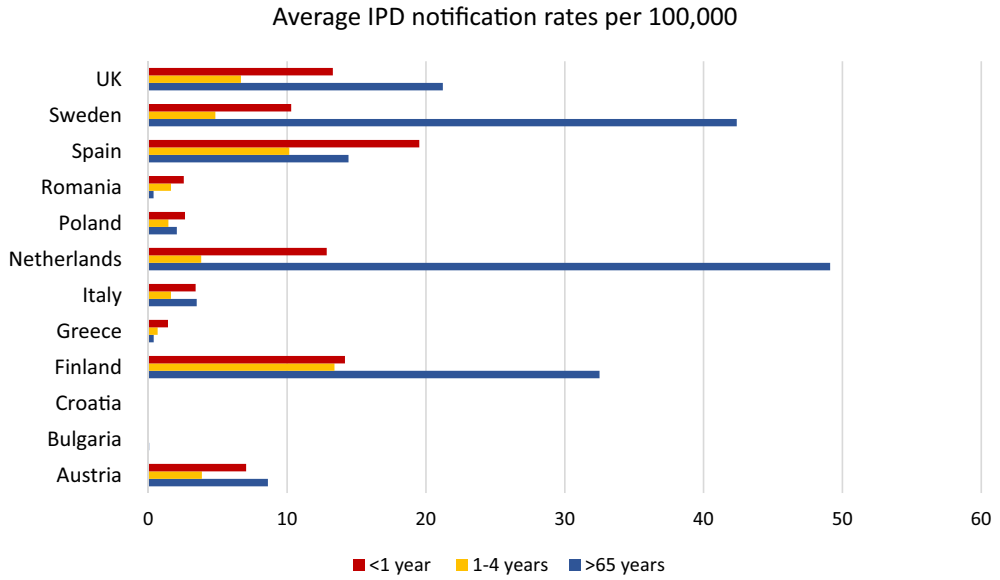

Fig. 5. Average notification rates for IPD in infants, young children and older adults.

Although most countries have a NITAG in place, its role varies, and while the majority of countries have a systematic framework in place for assessment, there is a range of approaches to the evaluation of data on vaccine safety and efficacy. Indeed, NITAG assessments and frameworks [6] appear to have no bearing on implementation timelines. While this may lead to some vaccines being implemented in a quick timeframe, the reasoning behind this decision-making is not always clear. As a result, other vaccines may not be considered. For example, countries that implemented horizon scanning for vaccines were not necessarily early implementers of vaccine UMVs in this analysis. Bulgaria was the first country in the analysis to implement a paediatric pneumococcal UMV, and Belgium, the first to implement a rotavirus UMV. Neither of these countries, however, use horizon scanning, a standardised approach, a systematic literature review, nor, consider health economic evidence as part of their vaccine assessment. The diversity in approaches to evidence also extends to economic evaluation, where cost-effectiveness isn't always included in the recommendation development process and, with a minority of countries considering the existence of a cost-effectiveness threshold as important prior to vaccine introduction.

The limitations of this research include the consideration of only a sub-set of countries within Europe and the use of only publicly available national level data. Therefore, the data may not reflect within-country variations, or the situation in countries with a decentralised approach to decision-making and implementation (e.g., Spain and Italy) and some data were not accessible. The data available at the time of collection may already have changed affecting the results, and there were differences in robustness and timeliness of publicly available data across countries and parameters (e.g., differences in time periods for analysis), limiting the value of cross-country comparisons. Among other factors that may influence VCR, vaccine supply was not considered and lack of availability of vaccine may result in a delay in UMV introduction. Given the

Table 4
National VCR achieved for primary DTP (infants), HPV (full course, adolescents) and Influenza (older adults).

	DTP (infants)			HPV (adolescents)		Seasonal influenza (older adults)		
	Age (months)	National VCR (%)	Range (%)	Age (years)	National VCR (%)	Age (years)	National VCR (%)	Range (%)
Austria [145,146]		98.0			NR	>65	32.1	
Belgium [145,147,148]		92.0	66.7–93.0	12–13	55.5	>65	66.1	59.2–65.8
Bulgaria [99,149]		92.1		12–13	14.1		NR	
Croatia [101,150]	Primary	95.0	87.1–99.1		NR	>65	30.0	
Finland [102,151,152]		98.2	95.9–100.0	11	68.8	>65	39.0	31.0–51.0
France [153–155]	9–24	96.7		15–16	19.1	>65	49.8	
Germany [111,112,156]	48–84	95.2	91.8–97.8	15–17	42.5	>60	35.3	20.1–55.7
Greece [115,157]	12	94.4	91.5–96.4	11–18	27.0	>65	29.9*	
Italy [116,158–161]	24	93.7	85.3–97.5	16	70.1	>65	52.0	
Netherlands [118,162]	12	93.5	89.6–97.5	14	53.0	>60	50.1	
Poland [120,163]	12	97.6		≤20	23.0	>65	4.3	
Romania [18,144,164,165]		89.1			NA	>65	14.9	
Spain [166]	12	96.6	94.8–100.0	11–14	79.0	>65	56.1	29.7–65.5
Sweden [128,167,168]	24	98.2		10–12	80.0	>65	50.0	35.0–62.0
Switzerland [75,131]	24	95.7	95.0–97.0	11–14	51.0		NR	
UK [137,138,169]	12	93.7	93.2–97.1	12–13	85.9	>65	71.6	66.6–74.5

* Percent in Greece refers to entire population, not just elderly; DTP: diphtheria tetanus pertussis; HPV: human papillomavirus; NA: Not applicable; NR: not reported; UK: United Kingdom; VCR: vaccine coverage rate.

primary interest in bringing together a range of datasets in this analysis, we have been unable to give sufficient depth to many of the issues raised, on which much has been previously written. Similarly, we were not able to augment our results for each country in the dataset with expert interviews and perspectives.

This analysis shows limited adoption and implementation of the EVAP 2015 to 2020 objectives to date, including setting common vaccination KPIs and goals across Europe. EVAP took a holistic approach to immunisation, seeking to steer a path towards ensuring long term domestic function of and political commitment to immunisation. On the whole, despite EVAP, more fundamental issues need to be addressed to improve country UMV performance e.g., increasing VCR and defining VCR goals in the target population.

In conclusion, these findings clearly reflect an individual approach to vaccination by country. Despite use of different assessment approaches, targets and underlying reporting systems, most countries could achieve high VCRs, particularly for paediatric vaccinations. Data on VCRs and targets show a continued prioritisation of paediatric immunisation in the majority of countries. Although national targets and EU- and WHO-Europe goals exist, the VCRs achieved are highly variable, reflected by the wide incidence ranges observed for vaccine-preventable diseases (e.g., MMR). Additional measures to improve VCRs across all age groups are needed and could benefit from greater harmonisation in data collection (e.g. EIRs and CRs) and sharing across EU countries.

5. Disclosures

5.1. Contributorship

SS, SC, CMa, SM and NB participated to the conception and design of the analysis, EB, EM, CMe and OS performed the research and collected the data. All authors were involved in the analysis and interpretation of the data. All authors had full access to the data and gave final approval before submission.

5.2. Funding

GlaxoSmithKline Biologicals SA funded this research and was involved in all stages of research conduct, including analysis of the data. GlaxoSmithKline Biologicals SA also took in charge all costs associated with the development and publication of this manuscript.

5.3. Disclosure of interest

SS, SC, CMa and SM are employees of the GSK group of companies and hold shares in the GSK group of companies. At the time of study conduct and during the whole development of this manuscript, NB was an employee of the GSK group of companies and holds shares in the GSK group of companies. CMe and OS are employees of Deloitte which received fees for the conduct of this research. At the time of the study conduct, EB and EM were employees of Deloitte. EB is now employed by ICF and EM is a research fellow at Maastricht School of Management. OD reports personal fees from the GSK group of companies during the conduct of the study; grants from the Robert Koch Institute and personal fees from the GSK group of companies, Sanofi Pasteur MSD and AstraZeneca outside the submitted work. MP reports grants and personal fees from various pharmaceutical companies, outside the submitted work and declares ownership of stocks in Ingress Consultancy. AP reports personal fees from the GSK group of companies for taking part in the advisory board related with this manuscript. OL discloses being an investigator for vaccine clinical trials with several pharmaceutical companies with remuneration to her organism and received personal fees for boards participation. TS has nothing to disclose.

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All authors attest they meet the ICMJE criteria for authorship.

Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.vaccine.2018.06.044.

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