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**DEVELOPMENT OF A VACCINATION REGISTRY IN GERMANY BASED ON
A COMPARATIVE SURVEY OF VACCINATION REGISTRIES IN EUROPEAN
COUNTRIES**

**RAZVOJ REGISTRA CEPLJENIH OSEB V NEMČIJI NA PODLAGI
PRIMERJALNE RAZISKAVE REGISTROV CEPLJENIH OSEB V EVROPSKIH
DRŽAVAH**

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I performed my master's thesis at the University of Ljubljana under the mentorship of Assoc. Prof. Mitja Kos, M. Pharm., Ph. D. and Prof. Dr. Klaus Wahle.

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Declaration

I declare that I performed the master's thesis alone under the mentorship of Assoc. Prof. Mitja Kos, M. Pharm., Ph. D. and Prof. Dr. med. Klaus Wahle.

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ABSTRACT

Introduction: Vaccination coverage is an indirect measurement of population immunity against vaccine-preventable diseases and is also one of the key performance indicators of a well-functioning immunization programme. To successfully close the gaps in the vaccination coverage and be able to evaluate the effectiveness of the vaccination strategies is essential, that reliable and accurate data, covering the whole population, are available timely. Vaccination registries can deliver such data, which can be further also used in vaccine effectiveness and safety studies as well as epidemiological studies. They include information on all administered vaccines, covering the whole population in a given geopolitical area. In Germany, there is no vaccination registry.

Aim of the study: To make an overview of the existing vaccination registries in Europe and based on the collected information, develop a concept of a vaccination registry in Germany, concerning the federal political structure, legal base, and immunization policy.

Methods: A questionnaire-based study. Target population: Thirty European countries.

Results and discussion: Twenty countries were included in the final analysis. In thirteen, vaccination registry exists. Eight of them have a national registry, three countries (more) sub-national and two, both kind. In our concept of a vaccination registry in Germany, every administered vaccine is recorded in electronic patient management system such as an electronic health record. This information is near real-time transferred through interfaces to one of the sixteen state-level sub-national registries, which have common technical standards and determined mandatory minimum data set to be collected. The data from the registries are transmitted to the national database at the Robert Koch Institute in a standardized format. The information collected must be fully anonymized, without a possibility of re-identification. Minimum data to be collected on single vaccination event are the year of birth and postal code of the place of residence of the vaccinee, date of administration, the name of the product, the batch number, and dose schedule. Obligatory and immediate reporting ensures completeness and timeliness of the data.

Conclusion: This study can raise awareness of the importance and benefits of vaccination registries by the stakeholders as well as promote their establishment in Germany and thereby improve the vaccine-preventable disease surveillance.

Keywords: Vaccination registry, Germany, vaccination coverage estimation, health informatics, vaccine-preventable disease surveillance.

POVZETEK

Uvod: Precepljenost prebivalstva je posredno merilo imunitete prebivalstva proti boleznim, ki jih je mogoče preprečiti s cepljenjem. Poleg tega je eden izmed ključnih kazalcev uspešnosti dobro delujočega programa cepljenja. Zanesljivi in točni podatki o precepljenosti, ki zajemajo celotno populacijo, so temelj za odpravljanje vrzeli v precepljenosti in za ocenitev učinkovitosti strategij cepljenja. Take podatke nam lahko zagotovi register cepljenih oseb. Ameriški centri za nadzor in preprečevanje bolezni (Angl. Centers for Disease Control and Prevention, CDC) te registre opredeljujejo kot zaupne populacijske računalniške baze podatkov, v katerih so zabeleženi vsi dani odmerki cepiv, ki jih prejmejo osebe določenega geopolitičnega območja. V kolikor register cepljenih oseb zagotavlja točne, zanesljive in izčrpne podatke o precepljenosti prebivalstva, se le-ti lahko uporabljajo kot vir podatkov za namene (i) spremljanja precepljenosti prebivalstva na regionalni in nacionalni ravni ter v posameznih skupnostih, (ii) zvišanja in vzdrževanja visoke precepljenosti z identifikacijo necepljenih posameznikov ali skupin, (iii) preprečevanja izbruhov bolezni, ki jih je mogoče preprečiti s cepljenjem z identifikacijo območij ali skupnosti z nizko stopnjo cepljenja, (iv) pravočasne prilagoditve priporočil za cepljenje, (v) podpore pri oblikovanju politike cepljenja, (vi) izvajanja ustreznih kampanj cepljenja, (vii) evaluacije strategij cepljenja, (viii) epidemioloških študij in študij učinkovitosti ter varnosti cepiv, itd. Poleg tega, dobro uveljavljeni registri cepljenih oseb izvajalcu cepljenja z izpisom pacientove zgodovine cepljenja nudi podporo pri določanju in načrtovanju ustreznih cepljenj, prepreči nepotrebna dvojna cepljenja in z napr. generiranjem opomnikov olajša načrtovanje nadaljnjih. Z vsem tem pa neposredno koristi pacientu, saj mu zagotovi vsa ustrezna cepljenja.

V Nemčiji takšnega registra zaenkrat še ni. Zbrani podatki o precepljenosti in o vrzelih v precepljenosti prebivalstva so trenutno na voljo le v omejenem obsegu. Zanesljivi podatki niso na voljo pravočasno ali pa so dosegljivi le za del prebivalstva.

Namen naloge: Namen naloge je bil s pomočjo vprašalnikov napraviti pregled obstoječih registrov cepljenih oseb v državah Evropske unije, na Norveškem in Islandiji ter v Liechtensteinu in Švici. Na podlagi zbranih informacij smo želeli razviti predlog registra cepljenih oseb za Nemčijo z upoštevanjem tamkajšnje politične strukture, pravne podlage, politike cepljenja in zdravstvene IT infrastrukture.

Metode: Po pregledu literature smo razvili dva raziskovalna vprašalnika. Enega za države, kjer register cepljenih oseb obstaja in enega za države, kjer tovrstnega registra (še) ni. Seti,

po dva vprašalnika, so bili razposlani v države interesa, najpogosteje na inštitucije javnega zdravstva. Z vprašalniki smo ugotavljali kakšno geopolitično območje pokriva register; kateri podatki o cepljeni osebi in o posameznem cepljenju se zbirajo; kdo ima dostop do registra; kako so generirani matični podatki; kakšne so njegove funkcije; namen uporabe zbranih podatkov; ali države poleg registra uporabljajo dodatne metode za zbiranje podatkov o precepljenosti prebivalstva; ali je poročanje v register obvezno in kakšne so sankcije, v kolikor poročanje ni opravljeno. Raziskovali smo tudi ali je uvedba registra cepljenih oseb vplivala na stopnjo precepljenosti prebivalstva in na kakšen način, ter sposobnost identifikacije kohort in regij z nizko stopnjo precepljenosti pri posameznih državah.

Rezultati: V končno analizo je bilo vključenih dvajset držav od katerih smo prejeli odgovor. Register cepljenih oseb obstaja v trinajstih državah. Osem jih ima nacionalni register (Danska, Finska, Malta, Nizozemska, Norveška, Slovenija, Švedska), tri države imajo podnacionalne (Belgija, Irska, Italija in Portugalska), dve (Islandija in Wales) imata obe vrsti. V petih od sedmih držav, kjer tovrstnega registra še nimajo (Bolgarija, Estonija, Francija, Liechtenstein, Nemčija, Slovaška in Švica), je le ta v razvoju. Med temi državami Nemčije ni.

Države z registrom so poročale o zvišani oziroma o nespremenjeni precepljenosti prebivalstva, znižanj ni bilo. Vse, razen Malte, lahko prepoznajo kohorte s prenizko precepljenostjo ter vse, razen Italije, lahko prepoznajo regije s prenizko precepljenostjo. Dvanajst držav podatke zbrane z registrom uporablja za razvoj nacionalnih priporočil in programov za cepljenje ter za oceno učinkovitosti nacionalnih programov cepljenja; sedem za ugotavljanje učinkovitosti in varnosti cepiv; osem za raziskovalne namene in šest za rekrutiranje posameznikov, vključenih v register v nadaljnje raziskave. V petih državah lahko register cepljenih oseb generira vabila k cepljenju in v šestih opomnike za potrebna nadaljnja cepljenja. V štirih primerih lahko register predvidi ustrezen načrt cepljenja za posameznega pacienta in v sedmih ustrezno prilagodi datume cepljenja, v kolikor je bilo cepivo dano prepozno in prav tako sedem jih ima funkcijo za upravljanje zaloge cepiv. Dva imata funkcijo upravljanja terminov za cepljenje in v treh primerih se v registru lahko zabeležijo razlogi za izpuščeno cepljenje.

Razprava: Z odgovorom na vprašalnik je Nemčija potrdila, da registra cepljenih oseb tam ni in trenutno tudi ni v razvoju. Kot razlog za to, je anketirana oseba navedla decentralizirani zdravstveni sistem ter pomisleke o zaupnosti podatkov. S tem je bila naša

domneva potrjena in razlog za to nalogo upravičen. Razvoj registra cepljenih oseb je v Nemčiji smiseln, saj predstavlja možnost izboljšanja trenutne situacije na področju razpoložljivosti podatkov o precepljenosti prebivalstva. V konceptu registra cepljenih oseb za Nemčijo, za katerega smo se odločili na podlagi zbranih informacij o že obstoječih registrih v evropskem prostoru in bi bil primeren za nemško politično okolje, zdravstveno politiko in zahteve o varstvu podatkov, smo sklenili slednje: Vsako dano cepivo je zabeleženo v elektronski sistem za upravljanje s pacienti, kot je na primer elektronska zdravstvena kartoteka. Ta informacija je preko vmesnika prenesena v enega od šestnajstih (za šestnajst zveznih držav) podnacionalnih registrov. Na ta način zvezne države ohranijo svojo suverenost. Ti registri imajo skupne tehnične standarde, kar olajša kompatibilnost in izmenjavo podatkov, določen je obvezen najmanjši podatkovni sklop, ki ga je potrebno zbirati. Podatki iz teh registrov, v obliki standardiziranega poročila v skoraj realnem času, hranijo nacionalno bazo podatkov na Inštitutu Robert Koch, ki je osrednja vladna znanstvena ustanova na področju biomedicine in katere naloga je razvoj konceptov, izvajanje epidemioloških in laboratorijskih analiz z namenom preprečevanja in širjenja nalezljivih bolezni ter njihovo zgodnje odkrivanje. Informacije, zbrane v registrih, morajo biti v celoti nepovratno anonimizirane. S tem sistem ustreza strogim merilom varstva podatkov. Najmanjši podatkovni sklop, ki ga je potrebno zbrati o posameznem cepljenju, je leto rojstva ter poštna številka kraja prebivanja cepljene osebe, datum cepljenja, ime ter številka serije cepiva in razpored odmerka (npr. primerni, poživitveni). Obvezno in takojšnje poročanje zagotavlja popolnost in pravočasnost zbranih podatkov. Funkcija generiranja opomnikov in vabil k cepljenju je bila prepoznana kot zelo koristna, zato predlagamo, da elektronski sistem za upravljanje s pacienti to vključuje. Poleg tega predlagamo vključitev funkcije, ki predvidi načrt za cepljenje glede na pacientovo starostno skupino ter funkcije, ki predlaga nadaljnje termine cepljenja in s tem, tako izvajalcu kot pacientu, olajša načrtovanje nadaljnjih cepljenj.

Zaključek: Ta naloga lahko zviša ozaveščenost zainteresiranih strani o pomembnosti in koristih registra cepljenih oseb ter prispeva k razvoju takšnega registra v Nemčiji. S tem bi izboljšali nadzor, epidemiološko spremljanje in preprečevanje bolezni, ki jih je mogoče preprečiti s cepljenjem.

Ključne besede: Register cepljenih oseb, Nemčija, ocenjevanje precepljenosti prebivalstva, zdravstvena informatika, epidemiološko spremljanje bolezni, ki jih je mogoče preprečiti s cepljenjem.

LIST OF ABBREVIATIONS

- ASHIP Associations of Statutory Health Insurance Physicians
- BE-WAL ISO-3166-2 entry for Belgium, Walloon Region
- BE-BRU ISO-3166-2 entry for Belgium, Brussels-Capital Region
- BE-VLG ISO-3166-2 entry for Belgium, Flemish Region
- CDC Centers for Disease Control and Prevention
- EHR Electronic health record
- Hib Haemophilus influenzae type b
- HIT Heard immunity threshold
- HPV Human papillomavirus
- IfSG Infektionsschutzgesetz, the Infection Protection Act
- IIS Immunization Information System
- JE Japanese encephalitis
- MenACWY Meningococcal disease, serogroups A, C, W135, Y
- MenC Meningococcal disease, serogroup C
- MenB Meningococcal disease, serogroup B
- MMR Measles, mumps, rubella
- PC Pneumococcal disease
- RKI the Robert Koch Institute, German federal government agency and research institute responsible for disease control and prevention
- SEE School entry examinations
- STIKO Ständige Impfkommision, German Standing Committee on Vaccination
- TBE Tick-borne encephalitis
- VC Vaccination coverage
- VPD Vaccine-preventable disease
- VR Vaccination registry

1 INTRODUCTION

1.1 VACCINATION COVERAGE AND ITS SIGNIFICANCE

Immunization prevents illness, disability, and death from vaccine-preventable diseases (VPDs) including cervical cancer, diphtheria, hepatitis B, measles, mumps, pertussis (whooping cough), pneumonia, polio, rotavirus diarrhoea, rubella, and tetanus. It is also one of the most cost-effective health measures (1). Due to vaccination, smallpox is an illness of the past, European region is sustaining polio-free status, and over the past two decades, a dramatic overall decline in measles and rubella was measured. However, recent measles outbreaks and increase in cases (2) (3) showed that some countries failed to achieve vaccination coverage (VC) rates required to prevent disease transmission and exposed gaps in country's ability to prevent and respond to such outbreaks (4).

VC (also immunization coverage) is calculated by dividing the number of the individuals who have received vaccination(s) within a given time (numerator) and the number of individuals eligible for it (denominator). It is an indirect measurement of population immunity against VPDs and determines the level of herd protection. When describing VC, the term 'full vaccination coverage' is used to describe the rate of individuals who received all recommended doses to achieve immunity.

To prevent ongoing transmissions and outbreaks of the VPDs, herd immunity thresholds (HITs) need to be reached throughout all communities in the whole region. Depending on the VPD, HITs are different. The more contagious the VPD, the higher the HIT. (5) However, this principle applies only to those VPDs which are contagious (tetanus is, for example, an infectious, but noncontagious VPD). Individuals who benefit from the herd immunity the most, are those who are unable to develop an immunity or those who cannot be vaccinated because of medical reasons.

VC is also one of the key performance indicators of a well-functioning immunization programme. It reflects the performance of the immunization services; it is used to guide the strategies for eradication, elimination, and control of VPDs, to identify areas of immunization systems that may require more attention and to assess the need for the introduction of new vaccines (6). To successfully close the gaps in the VC, to be able

to evaluate the effectiveness of the vaccination strategies and timely adjust the national vaccination recommendation is essential, that reliable and accurate data, covering the whole population, is available timely.

1.2 ESTIMATION OF THE VACCINATION COVERAGE

World Health Organization (WHO) describes two data sources for the estimation of the VC. It can be estimated by (i) conducting household surveys and (ii) using an administrative method, which is based on reports from service providers (7). For each type of data source, there are advantages and disadvantages.

The administrative data provide more timely information than data collected with household survey, however, to minimize the bias, the numerator and denominator estimates should be accurate. Under-reporting of the vaccinations from immunization units or non-inclusion of some vaccination sources (e.g., the private sector, non-governmental organizations) causes the numerator underestimation. Population migration, inaccurate population estimations and multiple sources of denominator data produce bias to the denominator. (7) The most significant underestimates occur in the areas with lowest reported coverage and the highest population mobility.

Data collected with household surveys allow estimating the VC even if the size of the target population is unknown and they also include vaccinations given by the private sector, for example. Conducting a representative and comprehensive survey is laborious, expensive, it takes time, and they provide information only on the previous birth cohorts. Therefore, they lack usefulness for timely programme interventions. Results in small samples may not permit for regional and local VC estimates and identification of the gaps (8). They are also subject to more errors, on account of possibly poorly trained interviewers, weak supervisions, erroneous analyses, respondent inability to recall and the length and complexity of the questionnaire may compromise the accuracy of the responses (6). Moreover, recruiting representative samples in telephone surveys is becoming harder with the time, due to the increase in the number of cell-phone-only households. Nonetheless, an essential advantage of these studies is their socio-demographic representativeness (9).

To collect, analyse and disseminate the relevant data, efficient and robust surveillance methods are required.

1.2.1 Estimation of vaccination coverage in Germany

In Germany, a single comprehensive system for VC estimation does not exist. Separate methods, covering different age groups, carried out to various extent and frequencies are used. They are (i) school entry examinations (SEE) and in some federal countries kindergarten entry examinations, (ii) Associations of Statutory Health Insurance Physicians (ASHIPs) vaccination monitoring project (KV-Surveillance) and (iii) population health surveys.

School entry health examinations

The collection of the data on the immunization status of the children collected as a part of school entry health examination (SEE) is the only method for VC estimation required by law (IfSG, §34(11)) (10). Depending on the federal state, the age of the children ranges from four to six years. Examinations are performed to check the completeness of the recommended childhood vaccinations. A presentable vaccination card is a prerequisite. The data of the children's immunization status are collected, aggregated and sent to the Robert Koch Institute, where the VC is calculated and annually published in the Epidemiological Bulletin. Representativeness, completeness, and validity of these data are high.

However, the newly introduced vaccinations are eligible for the assessment only several years after their introduction. Furthermore, since the SEEs take place after three to four years after the primary vaccination courses should be completed, the timeliness of vaccinations cannot be evaluated. That leaves the evaluation of recommended childhood vaccination completeness of high-interest target group, e.g., children at two years of age, unevaluated at the national level (9).

Associations of Statutory Health Insurance Physicians vaccination monitoring project (KV-Surveillance)

KV-Surveillance was established in 2004, as a joint project of the Robert Koch Institute (RKI) and the 17 Associations of Statutory Health Insurance Physicians

(ASHIPs). Quarterly, they provide the RKI with anonymous physicians billing data on the vaccine uptake of the statutory health insured individuals (around 85% of the population). The collection of this data started in 2004, so using this method the VC can be estimated for the vaccinations after that year. (9) Besides for the VC estimation, this method was also used to assess the effectiveness of varicella vaccines (11).

This method provides reliable data for infants, small children and pre-school children. For adolescents and adults, KV-Surveillance delivers merely reference points, since the ASHIPs cannot detect the person's doctor changes. Besides that, vaccinations administered in the scope of occupational health care, to privately insured patients (around 15% of the population) or self-payers (e.g., travel vaccinations) are not recorded at all.

Population health studies

Vaccination status is included as one of the multiple core indicators of population's health status in population health studies in Germany (*The German Health Interview and Examination Survey for Children and Adolescents (KiGGS)*, *the German Health Interview and Examination Survey for Adults (DEGS1)*, *the German Health Update Survey (GEDA)*). It is assessed for selected antigens based on a presented vaccination card, claims of the subjects themselves or by serological testing for specific antibodies. Depending on the sampling procedure the individuals are interviewed by telephone or invited to the study unit for a health examination or a face-to-face interview (health examination survey). They are conducted periodically, separately for children along with adolescents and adults. (9) Additionally to those mentioned above, sporadic and smaller studies for defined research questions are conducted by the RKI to gather information on knowledge, attitude, and behaviour towards vaccination in the general population or defined groups.

1.3 VACCINATION REGISTRY

Other terms used to refer to this electronic repository of immunization data are, e.g., vaccination registry (VR), immunization registry and Immunization Information System (IIS). US Centers for Disease Control and Prevention (CDC) defines these systems as confidential, population-based, computerized databases that record all immunization

doses administered by participating providers to persons residing within a given geopolitical area (12).

Well-established vaccination registries, benefit the public health institutions by continuously providing them with accurate, reliable and comprehensive data, which can be used as a single source of the data (i) to monitor the VC at the community, regional and national level, (ii) to increase and sustain high VC through identification of pockets of unvaccinated individuals or groups, age- and vaccine-specific, (iii) to prevent the outbreaks by identifying the areas and communities with low VC, (iv) to respond rapidly to the outbreaks and vaccine safety scares, (v) to make timely adjustments to the vaccination recommendations, (vi) to assist the development of vaccination and health policies, (vii) for the implementation of tailored vaccination campaigns, (viii) to audit the immunization strategies and activities as well as (ix) to safeguard the immunization records of individuals of over their lifetime. (13) (14) (15) (16) (17) They benefit the vaccine provider by providing them the consolidated immunization histories and thus facilitating determining appropriate and avoiding unnecessary double vaccinations; generating reminders and recall vaccination notices and assisting them with the scheduling process. They benefit the patient by ensuring him the appropriate vaccinations and allow them access to their vaccination history, through separate solutions. (18)

Crowcroft NS et al. put the importance of VC data in a publication *Registries: An essential tool for maximising the health benefits of immunisation in the 21st century*, very well into words, saying: “High-income countries have reached the point where such data are an essential part of any immunisation programme. While clinicians need good information on the protection of their patients to ensure a high standard of care, the individual citizen expects to be able to access their records as well, and public health authorities need to be able to identify and respond quickly to concerns to maintain the confidence of an increasing vaccine-hesitant public.” (19) Development of the vaccination registries across Europe is also very much advocated by the European Centre for Disease Control and Prevention (ECDC). In 2010, a European Conference on Immunisation Information Systems (ECIIS) was held. As one of its conclusions, it was recommended to develop a long-term EU plan to support the Member States to implement IIS able to communicate across the EU. ECDC supported that and added, that setting a goal to include over 75% of all European children and if possible also other age

groups in national IISs by 2020 would be valuable for monitoring of future EU vaccination programmes (17). Moreover, the Council of European Union invited member states to consider introducing or further developing of IIS (Council conclusions on childhood immunisation: successes and challenges of European childhood immunisation and the way forward) (20).

Besides achieving the functional requirements to deliver the complete, accurate and timely data, a VR must fit into country's environment conditioned by country's health system, vaccination policy, data protection requirements and IT infrastructure of the health sector.

1.3.1 Healthcare system, vaccination policy, data protection and existing IT infrastructure in health sector in Germany

1.3.1.1 Healthcare system and the stakeholders

Sharing of the decision-making between the federal states and the federal government is the fundamental characteristic of the German political and health care system. The exercise of state powers and competencies are assigned mostly to the federal states (*Article 30* of the German Constitution). The framework for health care is based on central decision-making. The Federal Ministry of Health is responsible for policy-making at the federal level. It also directs and oversees the self-governing activities within the healthcare system. The highest decision-making body within the self-governing healthcare system concerning statutory health insurance is the Federal Joint Committee (Gemeinsamer Bundesausschuss, G-BA). It is comprised of doctors, dentists, hospital representatives, representatives of the Statutory Health Insurer's organizations and patient representatives. It decides which, and in what extent the statutory insurers will cover medical services, it assesses new methods of medical examination and treatment, evaluates and classifies new drugs on the German market and is accountable for the publication of treatment guidelines and healthcare quality assurance as well. The Ministry of Health subsequently audits all resolutions and guidelines passed by the Federal Joint Committee. An independent federal Institute for Quality and Efficiency in Healthcare (IQWiG) was established for the evaluation of medical efficiency, quality, and effectiveness. It prepares non-binding recommendations to the G-BA (21).

1.3.1.2 Vaccination policy

The legal basis for the vaccination policy in Germany is mainly set by the Infection Protection Act (Infektionsschutzgesetz, IfSG), which's purpose is to prevent communicable diseases in humans, detect infections early and prevent their further spread (10). Vaccination is voluntary. Routine vaccinations and vaccinations for specific indications and target groups are publicly recommended by the highest health authorities in the federal states based on the recommendations of an independent advisory panel, the Standing Committee on Vaccination (Ständige Impfkommision, STIKO). STIKO develops national recommendations for the use of licensed vaccines (IfSG, §20(2)) (10). The recommendations are published annually in the Epidemiological Bulletin, a periodical of the Robert Koch Institute (RKI). These recommendations are no official government recommendations, and the federal states decide independently on their official recommendations, although they always follow STIKO recommendations closely. Vaccinations recommended by STIKO are reimbursed by statutory health insurances. Thus, they are offered free of charge. In Germany, health insurance is obligatory. Around 85% of people are insured with statutory health insurances and the rest with private insurance companies. All other administered licensed vaccines must be paid by the patients at their own expense.

According to the Infection Protection Act (IfSG, §22(1)) (10) are the administered vaccines recorded only in the paper vaccination card. Saxony-Anhalt is the only federal state with the statutory obligation to report the administered vaccines. However, there are no central guidelines on how to deal with the vaccination notifications received at the federal health department. (22)

The RKI is the government's central scientific institution in the field of biomedicine. It is one of the most important bodies for the safeguarding of public health. Its role under the Infection Protection Act is to develop concepts for the prevention of communicable diseases, their early detection, and prevention of the spread of infections, which includes the development and implementation of epidemiological and laboratory-based analyses as well as research into the causes, diagnosis, and prevention of communicable diseases. Furthermore, it supports the states and other stakeholders in their epidemiological surveillance tasks under this act (IfSG, §4(1-2)) (10).

1.3.1.3 Data protection

The Federal Data Protection Act (Bundesdatenschutzgesetz, BDSG) does not permit the collection of the personally identifiable data on the national level. Furthermore, it requires that any processing of the personal data requires explicit permission, be it by law or with the consent of the individual. (23)

Johansen K et al. highlighted the difficulties of development of a VR because of the data protection laws, and emphasised that it is vital to maintain public trust in such systems and to strike a balance between keeping the level of data protection high, while at the same time deliver the protection and promotion of health. In 2012, a reform of the EU's 1995 data protection rules was proposed to make Europe more fit for the digital age. The regulation was adopted on 27 April 2016, with enforcement date on 25 May 2018. This single act should reduce the current fragmentation in data protection laws across Europe, but it is difficult to say whether and how this will facilitate establishing the vaccination registries in EU countries with strict data protection laws (17).

The current data protection law orientates on data collection requirements, not on the context of their usage, which became relevant due to the new technical possibilities. In the Reform, a more significant involvement of the concept of *privacy by design* is highlighted. (24)

1.3.1.4 IT infrastructure

To electronically register the vaccinations and transfer the data to the VR, must vaccinating units be equipped with a solution that can do so. This solution could be a patient management software system, such as electronic health record (EHR)¹ being able to electronically record the vaccination and feed the VR with the data through interfaces or a separate solution for recording and transferring the vaccination data to the VR. In Germany, the improvement of the telematics in the healthcare sector promoted with the

¹ EHR is primarily considered as an electronic health record for integrated care (ICEHR), which is defined as [ISO/TR 20514, 2005]: "Repository of information regarding the health status of a subject of care, in computer process-able form, stored and transmitted securely and accessible by multiple authorized users, having a standardized or commonly agreed logical information model that is independent of EHR systems and whose primary purpose is the support of continuing, efficient and quality integrated healthcare".

E-Health Act, require all medical practices and hospitals to be connected to the telematics-infrastructure nationwide by mid-2018. By the end of that year, the prerequisites should be fulfilled, so that the data from the EHR could be transferred to an electronic compartment (patient has a sovereignty to decide if that is the case and what data is transferred), to which patients could access with the electronic healthcare card² outside of the doctor's office as well (25).

² Provided to every statutory insured individual.

2 AIM OF THE STUDY

The collected data on the VC rates and the vaccination gaps in Germany are currently available only to a limited extent. The data are either not available timely (Population health studies, SEE) or they deliver reliable data only for a part of the population (KV-Surveillance, SEE). To close the vaccination gaps in a timely and target group-specific manner, it is necessary, that the accurate information on the vaccination status of the whole population is available on a continuous and timely basis. A possible way to collect such data and thereby improve the VC rates is a VR. In Germany, there is currently no VR in use. The Conference of Ministers of Health in 2016 addressed this issue and in one of its conclusions asked the Federal Ministry of Health for a feasibility study for the establishment of a nationwide VR (26).

The aim of this study is (i) **to make an overview of the existing vaccination registries in countries of the European Union as well as Norway, Iceland, Liechtenstein, and Switzerland and their ability to serve their purpose** as well as (ii) **to provide a proposal for a solution for a vaccination registry in Germany.** We will study what surveillance systems countries use for the assessment of the vaccination status of their population, with the emphasis on the existence of a VR. The aim is to make an overview of the existing registries, learn best practices and expand the knowledge about the possibilities. We will collect information such as, which institutions have access to the VR; what data on the single vaccination event and the vaccinated persons is collected; what features does it have and what is the extent of the use of the data collected from it. We will determine their ability to serve their purpose by considering the impact of the implementation of the VR on the VC rates, country's ability to identify pockets of low VC, calculation of the VC for specific parameters (i.e., age, region) and country's need for other methods to estimate the VC. With the use of that information, a proposal for a solution for a VR in Germany will be developed concerning the federal political structure, legal base, and immunization policy, with the aim of achieving the highest possible benefit for the population.

3 METHODS

3.1 Population

30 countries (all member countries of the European Union as well as Norway, Iceland, Liechtenstein, and Switzerland) were invited per e-mail to participate in the survey about the surveillance systems for obtaining information on VC rates. England, Northern Ireland, Scotland and Wales of UK were invited separately, as well as Flemish, French and German communities of Belgium. We identified the respondents primarily by contacting the country's public health authority's, by contacting the authors of publications on relating topics and through referral.

In conclusion, we invited 30 countries to participate, yet we distributed 35 sets of questionnaires.

3.2 Research instrument

A questionnaire-based survey was identified as an appropriate method since we ought to collect information from a larger number of countries.

After a comprehensive literature review, we developed two research questionnaires; Questionnaire 1 (Q1) and Questionnaire 2 (Q2). The former was intended for the countries where one or more vaccination registries exist and the latter for the countries where it does not. They consisted of both, open- and close-ended questions. For a facilitated fulfilment of the survey, a set of answers was suggested, and the option "others" was always available as well.

A pilot study was not executed. Invitations for the research were sent out per e-mail in December 2016. There was no deadline. However, the responses were collected until the end of March 2017.

Questions I-IV of both questionnaires were the same and will be named *Common part of the questionnaires*. These four questions aimed to gain some general information on the country's vaccination programme. From the *Question V* onwards, the questions in the Q1 and Q2 differed.

Common part of the questionnaires

I: Respondents chose if country's health structure is centralized or decentralized.

II: Respondents chose the vaccinations that are included in the country's national immunization programme.

III: We asked whether the vaccinations are fully voluntary or, and if, which are compulsory.

IV: Respondents answered, if and which vaccinations are fully, partially or not reimbursed.

Research questionnaire 1 (Q1) from question V onwards

V: Respondents were asked to fill out the year of the implementation of the VR and name of the organization responsible for it.

VI: This section was asking about the information that is recorded in the VR. We asked what is the level of VR coverage (national, regional or local). In case of more local or regional registries present, we asked if they have common standards and requirements and whether it is challenging to obtain data on the national level and what are those challenges.

We inquired which vaccinations are included in the registry and in the next question, which information on the vaccination event is recorded, e.g., date of the administration of the vaccine, the product name, dose schedule (primary, booster series), etc. Furthermore, we asked how the master data in the VR is generated and which information on the vaccinee (a vaccinated individual) is recorded, e.g., name, date of birth, contraindications, health insurance status, identification number, etc.

VII: We inquired who can access the VR. E.g., Ministry of Health and other authorities, physicians, patients, etc.

VIII: This section consisted of three questions. We asked about the reporting to the VR. Whether it is mandatory, and what are the consequences (if there are any), if the vaccination is not reported. If each vaccination should be reported immediately and if there is an evaluation made on the comprehensiveness and quality of the reporting.

IX: In this section, the respondents were asked if any other means to calculate the VC are used and what are they. They were also asked if it is possible to identify the cohorts and regions with poor vaccination coverage and furthermore, whether it is possible to calculate the VC for any chosen parameter, and for which.

X: In this question, the respondents were asked about the uses of the data obtained from the VR. E.g., developing of immunization recommendations or programmes, evaluating

the effectiveness and impact of an immunization programme, monitoring the effectiveness and safety of the vaccine, research purposes, etc.

XI: This question asked about the features of the system. E.g., producing letters of invitation for the NIP, producing reminder letters, managing vaccination appointments, registering information on the reasons for missed vaccination, managing vaccine stock, etc.

XII: We asked if the VR is linked to any other registries, e.g., screening results registers and health outcome registers and which ones.

XIII: In this set of questions, we asked about the impact that the implementation of the VR had on the VC for MMR, Pertussis and Varicella vaccinations.

Research questionnaire 2 (Q2) from the question V onwards

V: In this section, we asked if there are any databases available for the recording of the administered vaccines or the recording of the immunization status and whether the recorded data are representative for the whole population.

VI: This question asked about the ways of calculating the VC in the country and limitations of those approaches.

VII: We asked if it is possible to identify the regions with poor VC.

VIII: We asked if it is possible to identify the cohorts with poor VC.

XI: We asked what are the limiting factors for not having a vaccination register. E.g., governance concerns, budget concerns, IT infrastructure not in place, decentralized health system, data confidentiality concerns.

X: Respondents were asked about their opinion on whether having a VR would be helpful for raising the VC in their country and why.

XI: We asked whether a VR is in development or not.

3.3 Data analysis

The research questionnaires were summarized and analysed in Microsoft Excel (Version 15.33). The validation of the data was not performed, which means that the respondents did not have the opportunity to recheck the answers after the final analysis.

3.4 Development of vaccination registry in Germany

From the collected information about existing vaccination registries, we will identify best practices and possibilities. With the support of the publications on the vaccination registries in the surveyed countries, we will develop a proposal for a possible structure and functionalities of a VR in Germany, concerning Germany's political structure, vaccination policy, data protection requirements and IT infrastructure in the healthcare sector.

We will conceptualize following aspects of the vaccination registry:

- *Coverage level of the vaccination registry*
- *Architecture of the vaccination registry and data flow*
- *Vaccinations included in the registry*
- *Information on a single vaccination event recorded in the registry*
- *Master data sources*
- *Access to the registry*
- *Reporting process*
- *Features of the registry*
- *Linkage to other registries*

4 RESULTS

Throughout this chapter, you will see a number in the brackets alongside every percentage presenting a result from the questionnaires, which represents the number of respondents and the percentage represented by it. E.g., 16 out of 21 responding countries, i.e., 76.2%, will be shown as 16 (76.2%). Geographical areas from where we received the response will be addressed as countries, though they, for example, include the regions in Belgium, which are not separate countries.

Research questionnaire response rate

We distributed 35 sets of questionnaires and received 21 in return (60% response rate) from 20 countries, which we included in the final analysis. 13 (62%) answered on the Q1 and 8 (38%) to the Q2. Table I and II represent countries, on behalf of the respondents completed one of the questionnaires and respondent's organization.

Background information for some countries

In **Belgium**, vaccination policy is a shared responsibility of the national Ministry of Health/Social Affairs and the regional authorities of the Flemish-speaking, the French-speaking, and the German-speaking communities. For that reason, we distributed the questionnaires to the local authorities and analysed the responses independently.

In **Italy**, 21 regional health authorities oversee organising and implementing own vaccination programme, based on the national vaccine plan. The questionnaires were sent only to the Italian Ministry of Health. The respondent provided us with the information that the situation in Italy (20 regions have a VR, one does not) fit in neither of the questionnaires and therefore filled-out Q1 from the national point of view. The answers were extracted from the Q2 and included in the analysis of the Q1.

We contacted and analysed public health authorities of England, Northern Ireland, Scotland and Wales in the **United Kingdom** separately as well.

Table I Responding countries and participating organization of the Questionnaire 1.

Belgium (Flemish Region)	Agency for Care and Health in Flanders, Prevention Division
Belgium (Walloon and Brussels-Capital Region)	The Office of Birth and Childhood
Denmark	Statens Serum Institut, Infectious Disease Epidemiology, and Prevention
Finland	National Institute for Health and Welfare, Department of Public Health

	Solutions
Iceland	Directorate of Health, Centre for Health Security and Communicable Disease Control
Ireland	HSE Health Protection Surveillance Centre
Malta	Ministry of Health, Primary Health Care
the Netherlands	National Institute for Public Health and the Environment, Centre for Infectious Disease Control
Norway	Norwegian Institute of Public Health
Portugal	Directorate-General of Health, Directorate of Disease Prevention and Health Promotion
Slovenia	National Institute of Public Health, Centre for Communicable Diseases
Sweden	The Public Health Agency of Sweden, Unit for Vaccination Programs
Wales, Great Britain	Public Health Wales

Table II Responding countries and participating organization of the Questionnaire 2.

Bulgaria	National Centre of Infectious and Parasitic Diseases, Department of Epidemiology and Communicable Diseases Surveillance
Estonia	Ministry of Social Affairs
France	French Public Health Agency, Infectious Diseases Department
Germany	Robert Koch Institute (The German National Public Health Institute)
Italy	Italian Ministry of Health, General Direction of Prevention
Liechtenstein	Office of Health
Slovakia	Epidemiology Department, Public Health Authority of the Slovak Republic, Epidemiology Department
Switzerland	Federal Department of Home Affairs, Federal Office of Public Health, Division of Communicable Diseases

4.1 Results of the research questionnaires

4.1.1 Common part of the questionnaires

4.1.1.1 Country's healthcare system

Bulgaria, Denmark, Estonia, Finland, Wales, Iceland, Malta, Norway, Portugal, Slovenia and Slovakia (11 (53.4%)) have centralized and Belgium, Switzerland, Germany, Ireland, Italy, Liechtenstein, Norway and Sweden (9 (64.3%)) have decentralized healthcare system. The respondent from the Netherlands checked both options.

4.1.1.2 Vaccinations recommended in the national immunization programme (NIP)

As of the time of the survey, all countries ((21) 100%) recommend immunisations with vaccines with DTP, Polio and MMR components in their NIP. Only one country does not recommend HPV vaccine ((20) 95.2%). Vaccines against pneumococcal disease (PC), hepatitis B, meningococcal disease serogroup C (MenC), influenza, and rotavirus are

recommended in 19 (90.5%), 15 (71.4%), 12 (57.1%), 11 (52.4%) and 9 (42.9%) countries respectively. Immunization against meningococcal disease serogroup B (MenB) as well as varicella are recommended in 4 (19.0%) countries; shingles and meningococcal disease serogroups A, C, W135, Y (MenACWY) vaccinations in 3 (14.3%); tick-borne encephalitis (TBE) in 2 (9.5%) and hepatitis A as well as rabies are recommended in one country 1 (4.8%). No country recommends vaccinations against Japanese encephalitis (JE), typhus and yellow fever.

Please refer to *Appendix 2* to see specific vaccinations recommended in the responding countries' national immunization programmes. Note that the response from Norway is based on the Childhood Immunization Program, although there are additional Influenza Immunization Program and HPV Immunization Program for elder women.

4.1.1.3 Compulsory vaccinations

As of the time of the survey, vaccinations are compulsory in Belgium, Bulgaria, France, Italy, Malta, Slovakia and Slovenia (8 (38.1%)) and fully voluntary in Switzerland, Germany, Denmark, Estonia, Finland, Wales, Ireland, Iceland, Liechtenstein, the Netherlands, Norway, Portugal, and Sweden (13 (61.9%)).

To see which vaccinations are compulsory in the countries with compulsory vaccinations, please refer to *Appendix 3*.

4.1.1.4 Reimbursement of the vaccinations

In 16 (76.2%) countries (Belgium, Bulgaria, Germany, Denmark, Estonia, Finland, Wales, Iceland, Ireland, Italy, Liechtenstein, Malta, the Netherlands, Sweden, Slovenia, Slovakia) vaccinations are entirely and in Switzerland and France partially reimbursed. Finland and Norway stated that there is no reimbursement, though, the respondent from Norway noted that the vaccinations from The Childhood Immunization Program are provided free of charge through public healthcare services and the respondent from Finland that the vaccinations that are part of the NIP (depending on region (e.g., TBE in Åland), age group (e.g., influenza for young children and the elderly), or sex (HPV for girls)) are offered free of charge. There was no answer from Portugal. Belgium, Walloon and Brussel-Capital region noted, that vaccination recommended in the NIP are fully

reimbursed within ONE structures (baby well clinics and day care centres). Other vaccines need a medical prescription and can be partially reimbursed (70-80%) by the mutual companies in relation to their supplementary sickness insurance activities. Portugal did not answer the whole question, and the Netherlands did not provide the specific information on which vaccinations are fully reimbursed.

To see which vaccinations are fully and partially reimbursed, refer to *Appendix 4*.

4.1.2 Questionnaire 1: Vaccination registry is in place

We received 13 Q1s in response, which describe a situation where one or more than one VR is present. To see which they are, please refer to *Table I*. As already mentioned before, Italy provided us with the Q2. However, it was included in this section.

Thus, we included 14 examples in this section of results.

4.1.2.1 Impact of the implementation of the vaccination registry on the vaccination coverage for chosen vaccinations

No country reported lower VC for any of the suggested vaccinations after the implementation of the VR. 7 (50.0%) and 2 (14.3%) of the countries reported higher and unchanged VC respectively for MMR as well as pertussis vaccination. 3 (21.4%) and 2 (14.3%) reported higher and unchanged VC respectively for varicella vaccination. There was no answer from 5 (35.7%) of the countries for MMR and pertussis and 9 (64.3%) for varicella vaccination.

The Netherlands, Sweden, Portugal, and Slovenia gave no answer this question. Dutch respondent explained that they did not study if the implementation of a VR had an impact on VC, but they expect no change because, before the introduction of the national registry, the same data were collected by nine separate offices in different registration systems. Swedish respondent noted that because the reporting is not yet complete, the data was not yet used for the VC calculation. The respondent from Portugal noted that such analysis was not made, but it is expected, that the VC is probably similar. However, its estimation is more accurate. Italy filled out the Q2, which did not include this question.

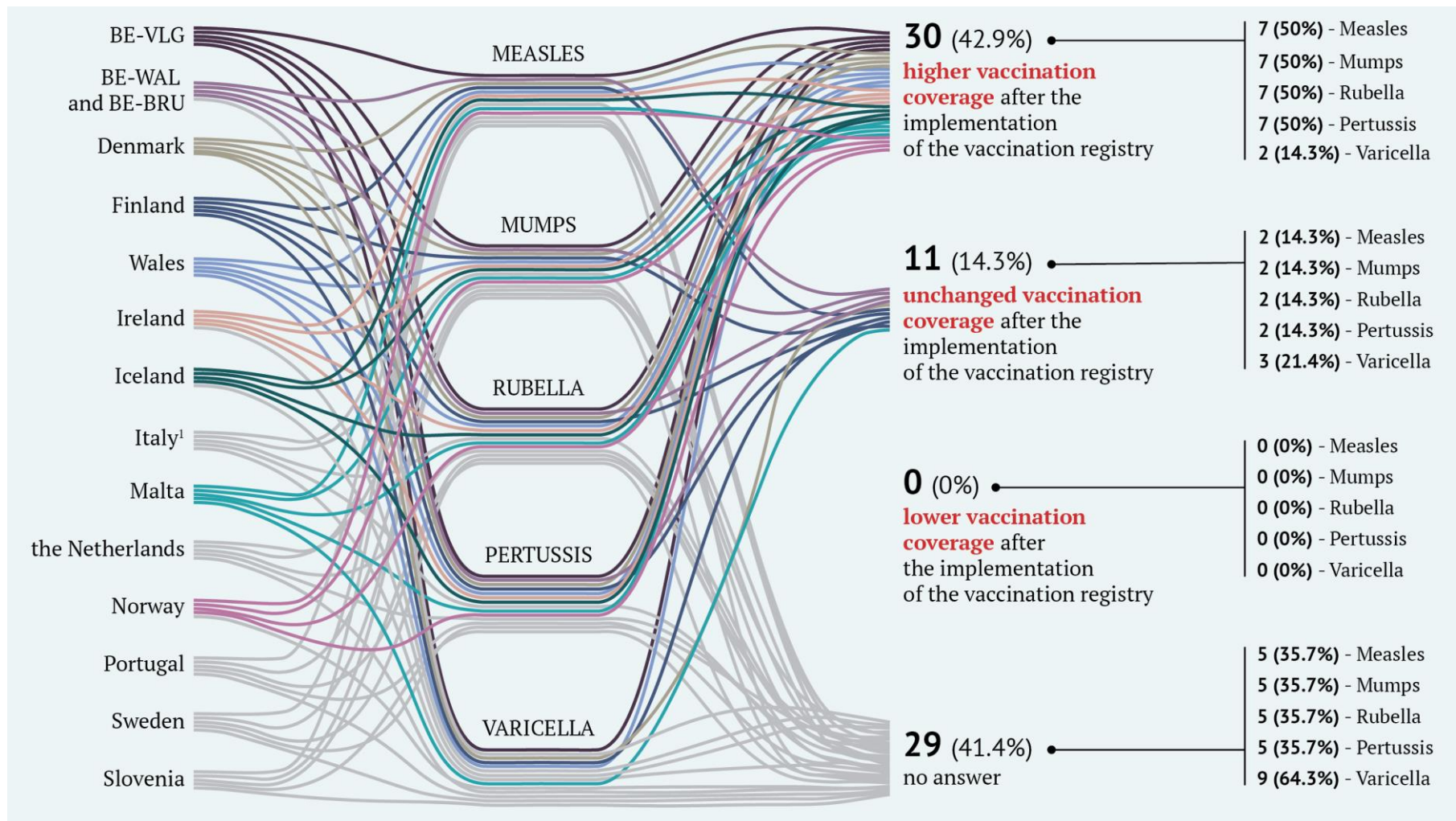


Figure 1 Impact of the implementation of the vaccination registry on the vaccination coverage for chosen vaccinations in responding countries. BE-VLG: Belgium, Flemish Region, BE-WAL and BE-BRU: Belgium, Walloon and Brussels-Capital Region. ¹ Italy filled out the Questionnaire 2, which did not include this question.

4.1.2.2 Possibility of identifying the cohorts and regions with poor vaccination coverage

All countries, except Malta 13 (92.9%) stated that they can identify cohorts with poor VC and all countries, except Italy can identify regions with poor VC.

4.1.2.3 Possibility of calculating the vaccination coverage for a chosen parameter

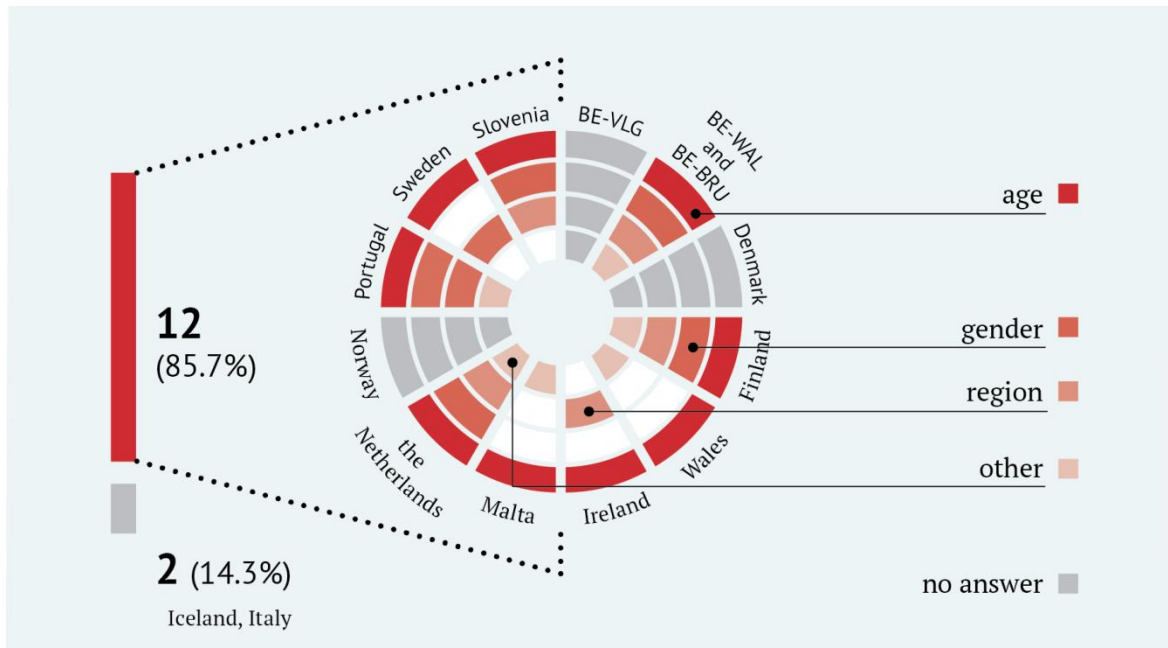


Figure 2 Possibility of calculating the vaccination coverage for age, gender, region and other parameters in responding countries. BE-VLG: Belgium, Flemish Region, BE-WAL and BE-BRU: Belgium, Walloon and Brussels-Capital Region. Other: Belgium, Walloon and Brussel-Capital Region: social and educational status; Finland: language, comorbidities, etc.; Wales: for LSOA (Lower Super Output Areas), GP practice; Malta: vaccine type; the Netherlands: country of birth of child/parents; Portugal: vaccine, doctor and administrative unit. Denmark, Norway did not explicitly state the parameters and Iceland did not answer to this whole question. Italy filled out the Q2, which did not include this question.

4.1.2.4 Other uses of the data obtained from the vaccination registries

Table III Other uses of the data obtained from the vaccination registries in responding countries, where a vaccination registry exists. BE-VLG: Belgium, Flemish Region, BE-WAL and BE-BRU: Belgium, Walloon and Brussels-Capital Region. ¹ Only allowed prior consent by the ethics committee. ² Others: BE-VLG: Communication on the homepage for the vaccinators. If necessary e-mailing to all or selected vaccinators as they must all have an actualized e-mail address in the registry; BE-WAL and BE-BRU: Financial reports.

	BE-VLG	BE-WAL and BE-BRU	Denmark	Wales	Finland	Ireland	Iceland	Italy	Malta	the Netherlands	Norway	Portugal	Sweden	Slovenia	
Developing of national immunization recommendations or programs	●	●	●	●	●	●	●			●	●	●	●	●	12 (85.7%)
Evaluating of the effectiveness and impact of a national immunization program	●	●	●	●	●	●	●		●	●	●	●	●		12 (85.7%)
Monitoring the effectiveness and safety of the vaccines	●		●	●	●		●			●	●		●	●	9 (64.3%)
Research purposes	●	●	●		●		●			●	●		●		8 (57.1%)
Recruiting individuals included in the vaccination registry for further research	●		●				●			●	¹ ●			●	6 (42.9%)
Others ²	●	●													2 (14.3%)

4.1.2.5 Other methods used for vaccination coverage estimation

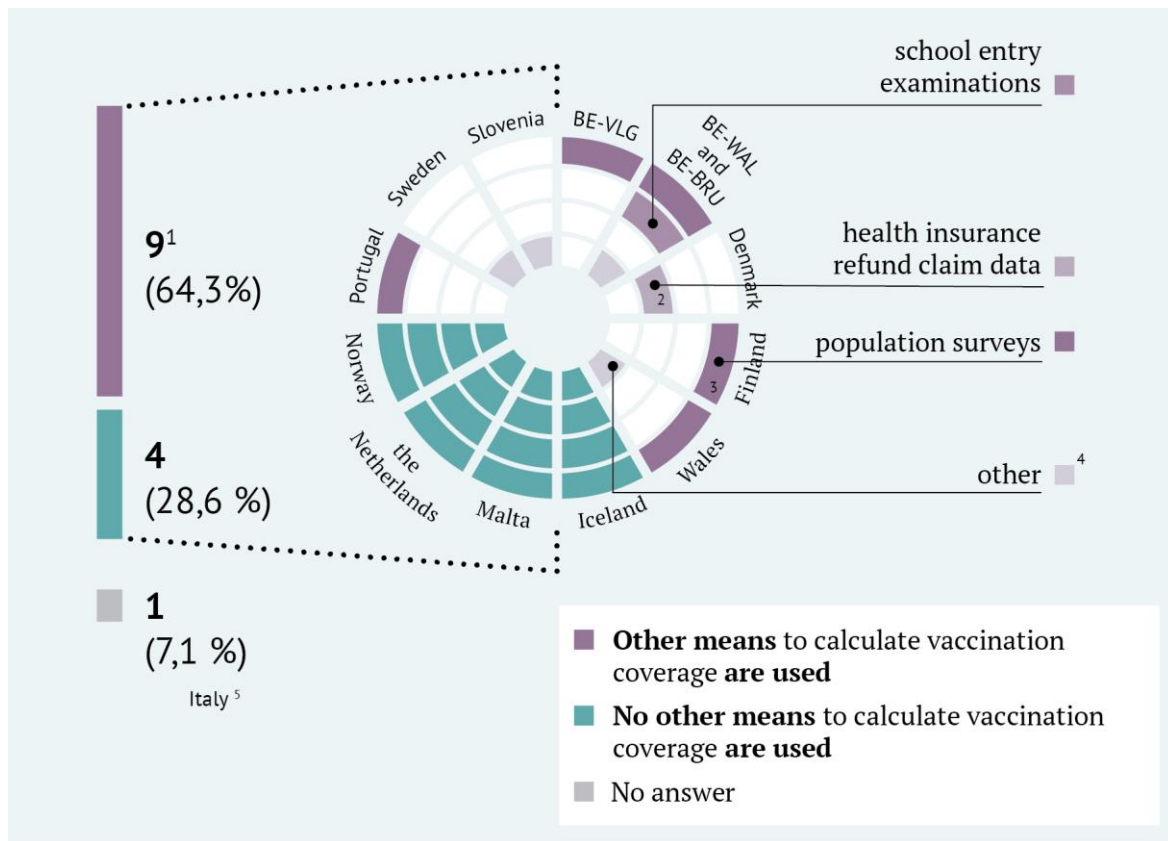


Figure 2 Other methods used for vaccination coverage estimation in the responding countries where a vaccination registry exists. BE-VLG: Belgium, Flemish Region, BE-WAL and BE-BRU: Belgium, Walloon and Brussels-Capital Region. ¹ Ireland did not specify what other means are used to calculate the vaccination coverage. ² Reimbursement codes from the regions. ³ Population and telephone surveys. ⁴ BE-WAL and BE-BRU: Data from Medical Social Data Bank (BDMS); Wales: Ad hoc surveys; Sweden: Yearly reporting from Child Health Care; Slovenia: Reports of health care providers with aggregated data on vaccinations performed. ⁵ Italy filled out the Q2, which did not include this question.

4.1.2.6 General information about the vaccination registry

Table IV General information on the vaccination registry (name, year of implementation and responsible organisation). Italy filled out the Questionnaire 2, which did not include this question.

	Name of the vaccination registry	Year	Responsible organization
Belgium, Flemish Region	Vaccinnet	2005	Agency for Care and Health in Flanders
Belgium, Walloon and Brussels-Capital Region	e-vax	2014	ONE ¹
Denmark	DDV, Det Danske Vaccinationsregister	2013 ²	Sundhedsdatastyrelsen
Finland	National Vaccination Register	2012	National Institute for Health and Welfare
Iceland	Vaccination Registry	2007	Chief Epidemiologist
Ireland	<i>Several registries at local level³</i>	1990 ⁴	Local HSE regions
Italy			
Malta	National Immunisation Programme	2008	National Immunisation Service
The Netherlands	Prøeventis	2005	RIVM/DVP, National Institute for Public Health and the Environment, Department of vaccine supply and prevention programmes
Norway	SYSVAK	1976 ⁵	Norwegian Institute of Public Health
Portugal	SINUS VACCINATION	2003	Ministry of Health
Slovenia	eRCO	2017	National Institute of Public Health
Sweden	The National Vaccination Registry	2013	The Public Health Agency
Wales	Community Child Health System / CCH2000/ CYPriS	1998 ⁶	Locally NHS health boards, centrally NHS national informatics centre

¹ An independent organ under the Ministry for Childhood of the Wallonia & Brussels Federation

² Implemented in 2013, from November 2015 the use of it became obligatory. The data on childhood vaccinations back from 1997 was uploaded into the system.

³ Multiple registries for primary immunization schedule in 8 different regions of the country. There is a secondary school immunization register for adolescent vaccines (HPV, MenC, and dTap) that was initially developed for pandemic influenza in 2009-2010, then modified to accommodate and meet the needs of the school-based immunization program for HPV and later extended to other vaccines (MenC and dTap).

⁴ since the 1990s- registries have been developed in the regions. A national registry is planned.

⁵ Introduced in 1976 as a trial project in parts of the country targeting the Childhood immunization program and further developed to cover nationally from 1995. From 1st of January 2011, it also includes other vaccinations (influenza, travel, work, diverse adult vaccinations).

Vaccinations can be registered retrospectively, so the registry also contains vaccinations given before these dates/years.

⁶More than 20 years ago.

4.1.2.7 Level of data coverage of the vaccination registry

Denmark, Finland, Malta, the Netherlands, Slovenia, and Sweden have national VR. Iceland, Norway, and Wales described their vaccination registries as that they cover all levels. Belgium, Ireland, Italy, and Portugal are countries with one or more than one sub-national (regional/local) VR.

In Belgium, there are two regional VRs; one covering the Flemish Region and the other Walloon and Brussels-Capital Region. They have common standards and requirements. Both respondents noted that they are based on the same software, which makes the data compatible. However, there are still some differences which should be solved to make the exchange of the data possible. The respondent from Flemish Region stated that the challenges with obtaining the data on a national level exist, however the respondent from Walloon and Brussels-Capital Region, that they don't.

In Wales as well as in Portugal the sub-national registries have common standards and requirements. In Wales, the collection of the data on the national level does not present a challenge; however, in Portugal it does, though the respondent did not explain what the problems are. In Ireland, the regional vaccination registries have common standards and requirements. Respondent noted that they are facing some challenges with the collection of the data on the national level, where they receive only the aggregated data. The systems are not connected, so for example, it is not possible to find out in one region if a child was vaccinated in another region without consulting someone in the other immunization office, who must check against name and date of birth.

Italy filled out the Q2, which did not include this question. However, the respondent explained, that there are regional vaccination registries in 20 of the 21 Italian regions.

4.1.2.8 Vaccinations included in the vaccination registry

Registries in Belgium, Flemish region, Denmark, Finland, Wales, Iceland, Malta, Norway, Portugal and Slovenia (9 (64.3%)) include more vaccination than just those recommended in the NIP. Five of those (BE-VLG, Denmark, Finland, Norway, and Portugal) can record all vaccinations against diseases suggested in the questionnaire. The

respondent from Norway noted that all possible vaccinations worldwide no matter when or where administered are recorded. Registries in the Netherlands, Ireland, and Iceland, 3 (21.4%) record all vaccinations included in the NIP. In Belgium, Walloon and Brussels-Capital Region, the only deviation from vaccination recorded and the NIP was the vaccination against rotavirus. Italy filled out the Q2, which did not include this question.

4.1.2.9 Information on each vaccination event collected in the vaccination registry

Table V Information on each vaccination event collected in the vaccination registry of each responding country. Italy filled out the Questionnaire 2, which did not include this question. BE-VLG: Belgium, Flemish Region, BE-WAL and BE-BRU: Belgium, Walloon and Brussels-Capital Region. Others: Norway: Standardized vaccination code. ¹ Not all fields are mandatory, due to the standardized vaccination code, e.g., batch number and product name.

	BE-VLG	BE-WAL and BE-BRU	Denmark	Wales	Finland	Ireland	Iceland	Italy	Malta	the Netherlands	Norway ¹	Portugal	Sweden	Slovenia	
Date of the administration	●	●	●	●	●	●	●		●	●	●	●	●	●	13 (92.9%)
Name of the vaccinator	●	●		●		●	●					●		●	7 (50%)
Name and location of the vaccinating unit	●	●	●	●	●	●	●		●	●		●		●	11 (78.6%)
Product name	●	●	●	●	●	●	●		●	●	●	●	●	●	13 (92.9%)
Batch number	●	●	●	●	●	●			●	●	●	●	●	●	12 (85.7%)
Manufacturer	●	●				●	●								4 (28.6%)
Dose schedule (primary, booster series)	●	●	●	●		●	●		●	●		●		●	10 (71.4%)
ATC code	●		●		●		●								4 (28.6%)
Side effects, if occurred	●	●					●					●		●	5 (35.7%)
Others											●				1 (7.1%)

4.1.2.10 Information on the vaccinee collected in the vaccination registry.

Table VI Information on the vaccinee collected in the vaccination registries of each responding country. Italy filled out the *Questionnaire 2*, which did not include this question. BE-VLG: Belgium, Flemish Region, BE-WAL and BE-BRU: Belgium, Walloon and Brussels-Capital Region. ¹ Address of the vaccinee concerns only the city and the zip code. ² Besides the date of birth, health visitor code, Health Authority (HA) of residence, lower super output areas (LSOA, the average population of 1,500) and middle super output areas (MSOA, the average population of 7,000) are recorded. They all resonate the district of residence. ³ The PIN includes information on age and sex. Through linkage with other registries, further information is available. ⁴ BE-WAL and BE-BRU: Age, gender, region, school grade; PT: observations.

	BE-VLG	BE-WAL and BE-BRU	Denmark	Wales ²	Finland	Ireland	Iceland	Italy	Malta	the Netherlands	Norway	Portugal	Sweden	Slovenia	
Name	●	●	●			●	●		●	●	●	●		●	10 (71.4%)
Date of birth	●	●	●	●	●	●	●		●	●	●		●	●	13 (92.9%)
Address	● ¹	●	●			●	●		●	●		●	●	●	10 (71.4%)
Contact (e.g. e-mail, telephone number)						●			●			●			3 (21.4%)
Health insurance status							●							●	2 (14.3%)
Contraindications						●			●						2 (14.3%)
Identification number	●	●	●		● ³		●		●	●	●	●	●	●	11 (78.6%)
Others ⁴		●										●			2 (14.3%)

4.1.2.11 Generation of the master data

Table VII Generation of the master data in the vaccination registries of the responding countries. Italy filled out the Questionnaire 2, which did not include this question. BE-VLG: Belgium, Flemish Region, BE-WAL and BE-BRU: Belgium, Walloon and Brussels-Capital Region. ¹ Others: Denmark: Statens Seruminstitut; Wales: Child health data collated in one local and national system. Adult immunisation data extracted from around 500 general practice databases and transferred to a central database using software called Audit+; Finland: National Institute for Health and Welfare.

	BE-VLG	BE-WAL and BE-BRU	Denmark	Wales	Finland	Ireland	Iceland	Italy	Malta	the Netherlands	Norway	Portugal	Sweden	Slovenia	
Automatically through data transfer from population registry	●	●	●			●	●		●	●	●	●		●	10 (71.4%)
By payers															0 (0%)
By health care provider												●	●		2 (14.3%)
Others ¹			●	●	●										3 (21.4%)

4.1.2.12 Access to the vaccination registry

Table VIII Access of different stakeholders to the vaccination registries of each responding country. Italy filled out the Questionnaire 2, which did not include this question. BE-VLG: Belgium, Flemish Region, BE-WAL and BE-BRU: Belgium, Walloon and Brussels-Capital Region. ¹ All vaccinations can be registered, and the system is also used by travel clinics. ² Only to the team at the NIPH. ³ Patient's access is being considered. ⁴ Others: Ireland: In local immunization offices, sometimes in some regions local public health offices also have access to the register, Malta: Well Baby Clinic and School Health staff; the Netherlands: Youth health personnel responsible for NIP execution; Portugal: Public health services; Slovenia: National Institute for Public Health.

	BE-VLG ¹	BE-WAL and BE-BRU	Denmark	Wales	Finland	Ireland	Iceland	Italy	Malta	the Netherlands	Norway	Portugal	Sweden	Slovenia	
Ministry of Health and other authorities	●		●	●	●				●	●	● ²	●	●		8 (57.1%)
Payer		●													1 (7.1%)
Physicians	●	●	●				●			●	●	●		●	8 (57.1%)
Nurse	●	●	●				●		●			●			6 (42.9%)
Patient to his vaccination record	●	³	●				●				●				4 (28.6%)
Guardian to children's vaccination record			●								●				2 (14.3%)
Others ⁴						●			●	●		●		●	5 (35.7%)

Norway noted that HCPs are not typically *nurses* or *physicians*, but healthcare stations, school care stations, general practitioner's offices, hospitals, vaccination clinics, etc. In Belgium, Flemish Region, patients can see their vaccination data from the registry on another general platform *Vitalink*, which is an exchange platform for medical data in Primary Health Care in Flanders. In Norway, patients can access their data and data of own children below 16 years of age in separate access solution is offered online through *My Vaccines*.

4.1.2.13 Reporting of the administered vaccines to the vaccination registry

Obligation to report

In 8 (57.1%) cases (BE-VLG, Denmark, Wales, Malta, Norway, Portugal, Sweden, Slovenia), the reporting to the VR is mandatory and in 4 (28.6%) cases (BE-WAL and

BE-BRU, the Netherlands, Ireland, Iceland) it is not. Finland did not define, but noted, that the National Vaccination Register is part of another registry (Registry of public primary health care visits) to which healthcare centres are obliged to report. However, the reporting of vaccines given outside primary public healthcare is therefore not mandatory.

Where the reported is mandatory, the respondents named the consequences if it is not:

Belgium, Flemish Region: The VR is linked to the vaccine ordering system. If vaccinations are not registered, the vaccine stock of free available vaccines will not go down (follow-up of vaccine stockpile), and consequently, vaccinators can't order the vaccines in the system anymore.

Denmark: It might generate reminder letter as if the patient didn't receive the vaccination.

Ireland: Non-payment of the vaccinator.

Malta: Regulation by Superintendent of Health.

Norway: In practice, none. However, the responsible team at NIPH has legal options, but they try to solve this through communication rather than sanctions.

Portugal and Sweden: No consequences.

Slovenia: According to the Law on infectious diseases Health Inspectorate can issue a decision to pay penalties.

Timing of reporting

In 12 (85.7%) countries (BE-WAL and BE-BRU, Denmark, Finland, Wales, Ireland, Iceland, Malta, the Netherlands, Norway, Portugal, Sweden and Slovenia), the administered vaccination should be reported immediately. In Belgium, Flemish Region (1 (7.1%)), immediate reporting is not necessary.

Evaluation of the comprehensiveness and quality of the reporting

8 (57.1%) countries (Belgium, Flemish region, Wales, Finland, Malta, the Netherlands, Norway, Portugal, Sweden) stated that they evaluate the comprehensiveness and quality of the reporting. 3 (21.4%) (Belgium, Walloon and Brussels-Capital Region, Ireland, Slovenia) do not. Italy filled out the Q2, where these questions were not included.

4.1.2.14 Linkage to other registries

In Denmark and Finland, VRs are not automatically linked. However, is possible if the permission is granted. In Finland, e.g., with Population Registry, National Infectious Diseases Register, Hospital Discharge Register, Register for Primary Healthcare visits, Medical Birth Register, etc. In Belgium, Flemish Region is not linked to any as well, but since the national number is used as the unique identifier, the data can be matched for research and other reasons. Belgium, Walloon and Brussels-Capital Region stated that the linkage is not yet possible. Iceland, Ireland, Malta, the Netherlands, Norway, Portugal, Slovenia, Sweden, and Wales did not answer this question; thereby the linkage is probably not possible. Italy filled out the Q2, which did not include this question.

4.1.2.15 Features of the vaccination registry

Table IX Features of the vaccination registries of the responding countries. Italy filled out the Questionnaire 2, which did not include this question. BE-VLG: Belgium, Flemish Region, BE-WAL and BE-BRU: Belgium, Walloon and Brussels-Capital Region. ¹ Electronic Patient Record (EPR) systems have these features. ² Vaccination registry is also a vaccine ordering system. ³ Follow-up of the number of vaccines ordered by type of vaccinator, e.g., GP, school health service, well-baby-clinic, paediatrician, etc.

	BE-VLG	BE-WAL and BE-BRU	Denmark	Wales	Finland	Ireland	Iceland	Italy	Malta	the Netherlands	Norway ¹	Portugal	Sweden	Slovenia	
Producing letters of invitation for NIP			●		●				●	●		●			5 (35.7%)
Producing reminder letters			●	●	●				●	●		●			6 (42.9%)
Managing vaccination appointments				●					●						2 (14.3%)
Foresight of the vaccination plan	●	●	●	●											4 (28.6%)
Vaccination plan adjustment	●	●	●	●					●	●		●			7 (50.0%)
Registering reasons for missed vaccinations				●					●			●			2 (14.3%)
Managing the vaccination stock	●	●			●				●	●		●		●	7 (50.0%)
Others	● ²	● ²													2 (14.3%)

4.1.3 Questionnaire 2: Vaccination registry is not in place

4.1.3.1 Databases for recording of vaccinations in the countries without the registry

In Bulgaria, health care claim database holds the information on administered vaccines; the vaccinations are also recorded in the GP's register book for immunizations and on the patient's vaccination card. In Germany and France, the healthcare claim database holds the information on the administered vaccines as well. In Switzerland, a web-based platform is used, which functions as electronic vaccination record. Liechtenstein records them in National Registry for preventive medical examinations, where vaccinations are included for children and youth. In Slovakia as well as in Estonia, vaccinations are registered only on paper immunization record, though in Estonia, an electronic one is also used.

All of them, except Liechtenstein, stated that the registered data are representative for the whole population.

4.1.3.2 Methods of vaccination coverage calculation and limitations of the approach

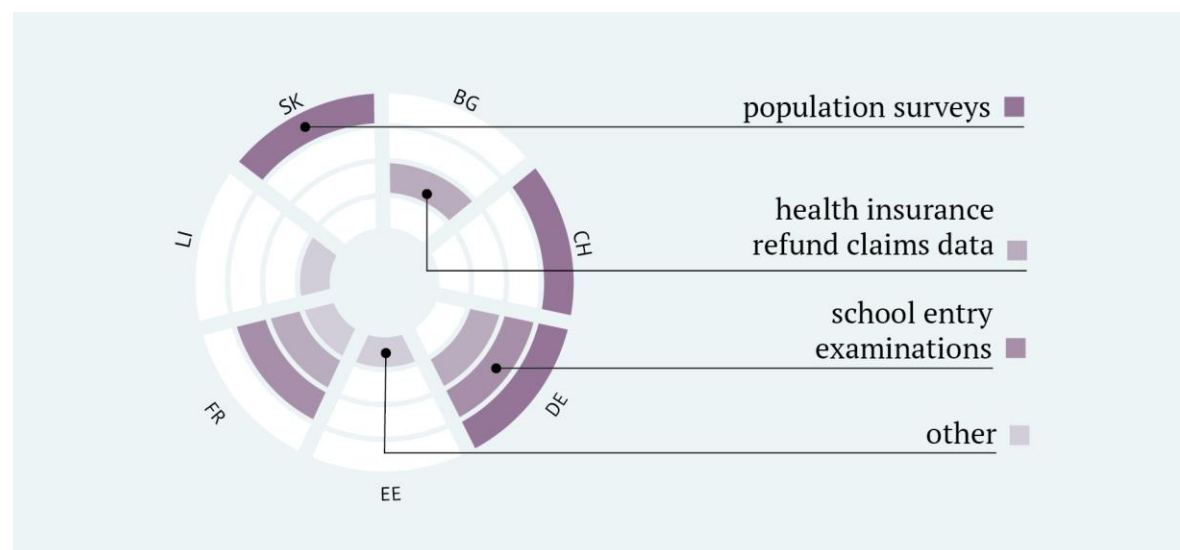


Figure 4 Methods for calculation vaccination coverage in responding countries without an existing vaccination registry. Other: Liechtenstein: The data from National Registry for preventive medical examinations, Estonia: Annual reporting by the health care providers, France: The data from health certificates, which are mandatory filled by the GPs/pediatricians for a child at nine months and two years of age.

Limitations of the approach:

France: The respondent noted that the health certificates are exhaustive to fill out and to transmit to the national level. There is a delay in adjusting the certificates' format to changes in the vaccination schedule, as well as the lag time between data availability is significant. Regarding the health care reimbursement database, the respondent noted, that it is quite comprehensive, though a small proportion of vaccines administered for free in public centers and Maternal and Child Health clinics are missing.

Liechtenstein: Reliable data exists only for children and youth up to the age of 16.

Estonia: The vaccinations not introduced in the NIP are probably underreported.

Germany: Some population surveys (especially telephone survey) are prone to bias (including reporting bias). *SEE:* The data covers only children who present their vaccination document; date/time of vaccination is generally not recorded; lag time between the recommended age of vaccination and reporting of coverage estimates and that vaccinations recommended after school-entry age cannot be considered. *Health insurance claims data:* The data covers only statutory health-insured population which is estimated to be ~85% of the population; data are initially recorded for reimbursement and not for epidemiological analyses and may contain errors; because of population migration, patients are selected from the data to perform cohort analyses, and thus this selection process may lead to selection biases.

4.1.3.3 Possibility of identifying regions or cohorts with low vaccination coverage

All countries, except Liechtenstein (Bulgaria, Estonia, France, Germany, Slovakia, and Switzerland) stated that they can identify regions with low VC. Identification of cohorts with low VC is possible in 4 (71.4%) cases (Estonia, France, Germany, Slovakia, and Switzerland) and 2 (28.6%) (Bulgaria and Liechtenstein) it is not.

4.1.3.4 Limitations for not having a vaccination registry

Bulgaria: Governance and budget concerns.

Germany: Decentralized health system and data confidentiality concerns.

France: Governance and data confidentiality concerns, IT infrastructure is not in place (the electronic files containing vaccination data remain at GP's/paediatrician's clinics level).

Liechtenstein: Governance and data confidentiality concerns.

Slovakia: Budget concerns.

Switzerland: IT infrastructure is not in place and decentralized health system.

In Estonia, the introduction of a national electronic immunization registration system is planned for the second half of 2017.

4.1.3.5 Status of vaccination registry development

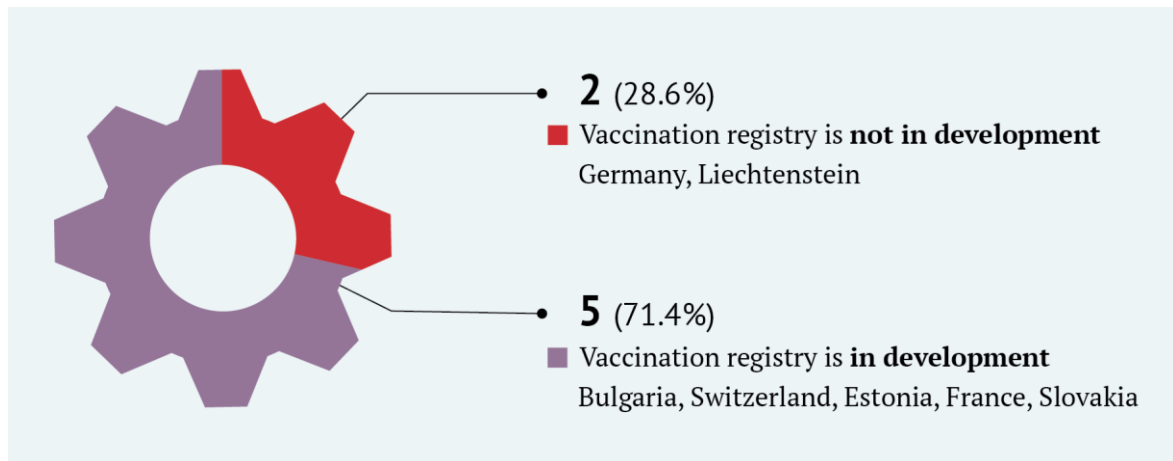


Figure 5 Status of vaccination registry development in the responding countries with no existing vaccination registry.

5 DISCUSSION

With the questionnaires, we aimed to determine whether vaccination registries contributed to the raising of the VC; if the countries that use the VR can identify pockets of suboptimal VC; estimate the VC for specific parameters (i.e., age, region) and whether other methods for VC estimation are needed.

No country reported lower VC for any of the suggested vaccinations (MMR, pertussis, and varicella). Many countries, from which we received the answer to this question, reported higher VC for MMR and a few unchanged VC. Some responding countries did not provide us with the answer for varicella vaccination. The reason for that could be that none of the countries which record varicella vaccination in the VR have varicella vaccination recommended in the NIP. Thus, varicella vaccination is not a point of interest for them for the VC estimation. Four countries did not answer this question at all. The most notable reason, for not answering this question we received from the Swedish respondent, who explained, that the reporting is not yet complete and therefore the estimation would be incorrect, which teaches us the importance of the comprehensive reporting of all administered vaccines. The respondent from Portugal noted that the VC is probably similar; however, the estimation is more accurate. Altogether we can say that the impact of the vaccine registry implementation on the VC was positive. The VC was either higher or unchanged to prior the VR introduction. However, there is no assurance that this is due to the VR implementation or any other reasons.

In 92.9% of the cases where the VR exists, it is possible to identify cohorts and regions with low VC. Furthermore, countries stated for what parameters it is possible to calculate the VC. All can do it for age cohort, and other stated parameters include, e.g., gender, region, GP practice, social, and economic status. That is of high importance, so appropriate targeted measures regarding raising the VC, outbreak prevention and control can be taken. However, we cannot be sure that exclusively data from the VR are used for that purpose since 71.4% of the countries still use additional methods (mostly the population health surveys) for VC estimation. Unfortunately, we did not request the clarification for that.

Besides the estimation of the VC, there are many other applications of data collected with the VR. Most of the countries (85.7%) use them for the development of the national immunization recommendations and programmes as well as to study their effectiveness and impact. Such data provide an extent to laboratory-based and case-based VPD surveillance systems, and therefore, they are valuable in the rational decision-making. Changes in the immunization programmes must rely on evidence-based decisions, and they should be performed carefully (17). Furthermore, it can be a valuable tool for evaluating vaccine effectiveness and safety in the phase of vaccine new introduction as well as for the long-term performance of the vaccines, and many countries (64.3%) use them for this purpose. One example of this found in the literature is the case, where the data from the Norwegian Immunisation Registry (SYSVAK) was used to estimate the vaccine effectiveness and describe vaccine failures during the influenza pandemic in Norwegian vaccine effectiveness study, following immunization against influenza A(H1N1)pdm09 (27). Another example is a Finnish study, which studied whether the onset of narcolepsy was due to a manufacturing error of some batches of an influenza vaccine since certain batch numbers occurred more frequently in patients who developed narcolepsy. Nationwide vaccination data from a VR were linked to information from patient files and proved no correlation (28). Similarly, the data can be used in the studies to investigate the vaccine safety scares and claims of adverse effects. E.g., in Sweden and Denmark, they investigated the occurrence of adverse events affecting adolescent girls after HPV vaccination (29). Where the data can be retrieved to the individual level, the individuals can be recruited for further research. E.g., in the Netherlands, Præventis includes both vaccinated and unvaccinated individuals. They can be requested by post, if they are willing to participate in specific studies, such as questionnaire-based studies on hepatitis B acceptance, studies with focus groups and vaccine effectiveness studies (30).

As we could see, a general impact of the vaccination on the VC was positive; countries can identify cohorts and regions with low VC; calculate it for different parameters and use the collected data for many different purposes.

5.1 Development of a VR in Germany

Germany responded us with a Q2 and confirmed that in Germany VR neither exists nor is one in development. In addition to that, similar limitations to the current methods for VC estimation used were presented as we suggested in the introduction. Thereby, the reason for our research was justified. As limitations for not having one, decentralized healthcare system and data confidentiality concerns were stated.

To achieve the highest functionality of the VR and to put the data collected with it, in superior and preferable position with the data obtained with current methods, must the data be complete and accurate, available timely and cover the whole population, regardless of their insurance status. They must be suitable for the monitoring of the VC and the use in epidemiological studies. If these requirements are fulfilled, VR could serve as a single valuable source of data for VC estimation.

When all administered vaccines in the whole population are registered in the VR, the data are complete. In Germany, there is no legal basis which would require registering administered vaccines in any electronic form. The only federal state with mandatory notification of vaccination to the Health Department is Saxony-Anhalt (22). To achieve completeness of the data, **must all vaccination providers be obligated to electronically register all administered vaccines in all federal states.** Therefore, every vaccinating unit should have access to a solution able to electronically register the vaccinations and transfer the data to the VR. Which could be a patient management software system, e.g., EHR being able to electronically record the vaccination and feed the VR with the data through interfaces or a separate solution for recording and transferring the vaccination data to the VR. As a part of the improvement of the telematics in the healthcare sector promoted with the E-Health Act, all medical practices and hospitals are required to be connected to the telematics-infrastructure nationwide by mid-2018. (25) **A prerequisite of integrating the VR within this eHealth initiative would, therefore, be including electronic vaccination records in the patient management system, e.g., EHR.**

The Federal Data Protection Act (Bundesdatenschutzgesetz, BDSG) does not permit the collection of the personally identifiable data on the national level. (23) **The data collected in the VR must be therefore anonymized** and follow the concept of *privacy*

by design. The anonymization process must assure that the data stored can no longer be assigned to individuals. For the main scope of data usage (i.e., VC estimation) are anonymised vaccination records sufficient. The processing systems for data storage must be strictly monitored and protected against access by unauthorized persons as well. The Federal Data Protection Act also requires that any processing of the personal data requires explicit permission, be it by law or with the consent of the individual (23). Therefore, the registering in the electronic patient record systems requires informed consent.

5.1.1.1 Coverage level of the vaccination registry

National vaccination registry

VR with the national level of coverage includes administered vaccination in the whole country in one central database. Countries with national VR are Denmark, Finland, Iceland (all levels), Malta, the Netherlands, Norway (all levels), Slovenia, Sweden, and Wales (all levels). Norway noted that SYSVAK is a national registry which covers all levels. On local level EPRs (Electronic Patient Record system) are used, where vaccinations are recorded, and the information is automatically transferred to SYSVAK.

Because the data are derived from one system that covers the whole country, and there is no need to combine several data sets extracted from sub-national, there are many advantages of having a national VR. It improves transparency and consistency of the VC data, and it simplifies its estimation. It simplifies the evaluation of the NIP as well and, the tracking of the immunization histories of individuals who change the residency is thereby improved. (30) (31)

Sub-national (regional/local) vaccination registry

VR with sub-national (regional/local) level of coverage includes administered vaccines in a defined area (e.g., region, local health units). Countries with sub-national VRs are Belgium, Portugal, Ireland, Italy, and Wales.

Though the data are of great importance for the vaccination programme monitoring on the sub-national level, the data of the same quality should be available on the national level. In all cases, sub-national VRs have common standards and requirements, although some still find it challenging to obtain the data on the national level. Common (functional)

standards and requirements, same software, mandatory minimum data sets which increase their interoperability, facilitate the collection of the data on the national level. We observed that the possibility of the data exchange between the registries is an important aspect as well. Ireland and Belgium noted that absence of data exchange possibility presents a challenge. Some countries with sub-national registries have formed interregional working groups and associations; determined common standards and data sets of the registries and have standardized national reporting of the data to reduce the complexity of the system and data compatibility and therefore, the collection of the data on a national level. In England for example, local health authorities - CHISs (Childhood Health Information Systems), which might have different extraction processes, data reports are standardized by COVER parameters (Cover of Vaccination Evaluated Rapidly programme) (32). In Italy, many vaccination registries on regional level exist, among which not all are interoperable. In 2007, an interregional working group defined a minimum set of variables to be included in local computerised registries, to enable the development of a national system capable of aggregating the data from all Italian regions (33).

It could be expected, that sub-national registries would be more commonly present in the countries with a decentralized healthcare system. All with centralized healthcare structure have either VRs on the national level or VRs covering all levels. Results showed that two countries (Belgium and Italy), who have decentralized healthcare system also have sub-national VRs, but they also showed, that two countries (Norway and Sweden) who also have a decentralized healthcare system, have implemented national VR. However, if the responsibility for the vaccination policy and immunization plan is considered, the correlation is more visible. In Norway, Sweden and other countries with a centralized health system, the programme is set and regulated on a national level, and it applies to the whole country. In Belgium and Italy, regional health authorities oversee the implementation of the immunization plan. They are also the only among the research countries where this is the case.

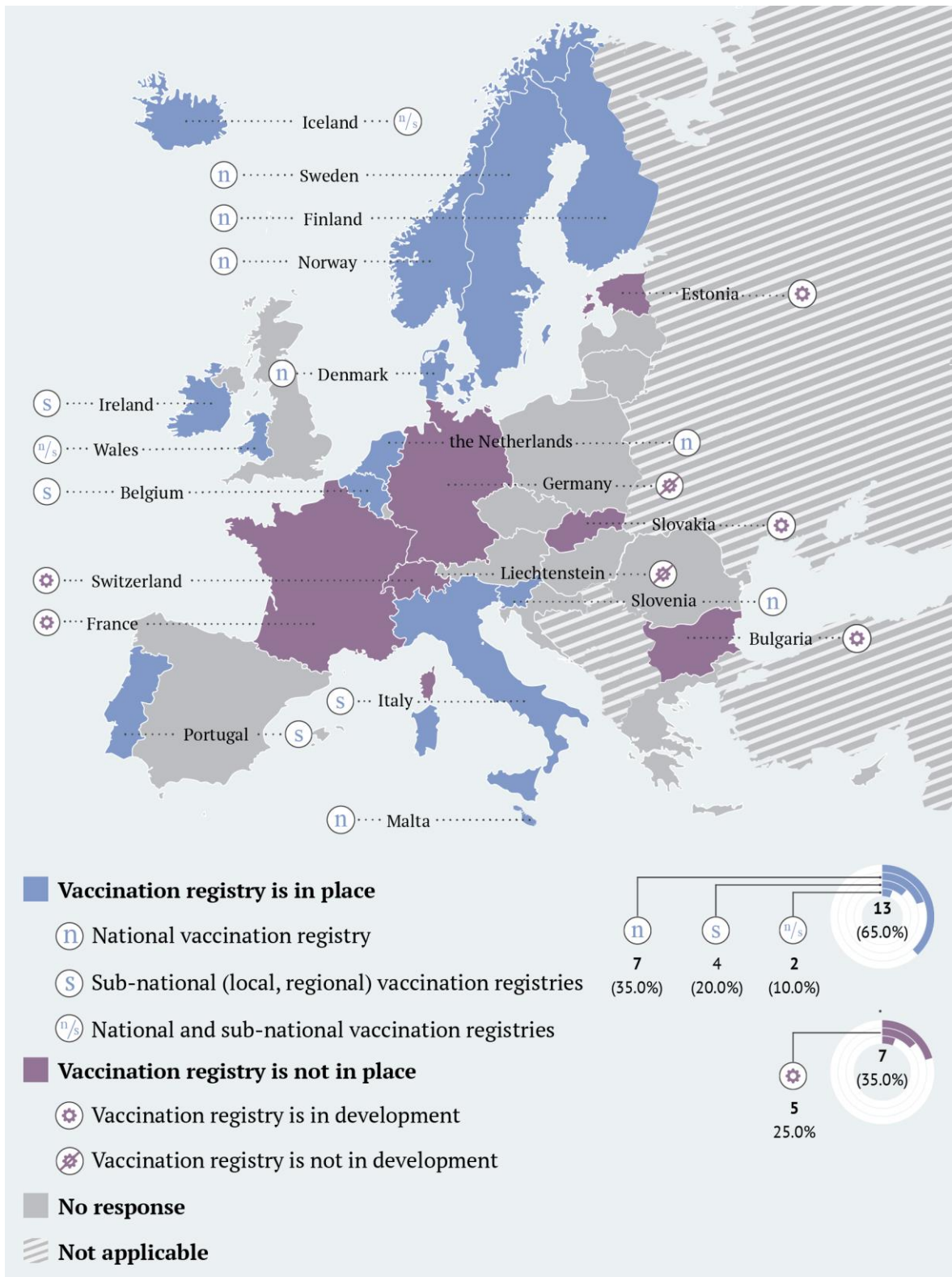


Figure 6 Vaccination registry presence status and level of coverage in responding countries.

A network of sub-national VR seems to be a suitable solution for Germany, with a decentralized healthcare system and the implementation of the vaccination program being in the hands of the Local Health Departments as well. We learned that the interoperability, data compatibility, and data exchange in the setting of more sub-national VR is vital. Since there is no existing VR in Germany yet, there is an excellent opportunity to determine the minimum set of standards, and the minimum required data to be collected with the VRs beforehand. Consequently, a high level of data compatibility on the national level can be achieved and still allow the states to collect additional data on the state level.

There are 16 federal states in Germany. Hence, *a network of 16 vaccination registries with common functional standards and requirements (e.g., mandatory minimum data to be collected, same software) covering their geographic jurisdiction.*

5.1.1.2 Architecture of the vaccination registry and data flow

For the architecture of the data flow, we decided on a setting as seen, e.g., in Norway, where vaccination data are transferred from the EPRs (electronic patient record system) at the GP's office to the SYSVAK through an interface; and in Denmark, where notification can be made either by integrating the DDV in the EHR system used or via an online solution (34), with the difference that the data would feed a sub-national, not a national VR. We believe that recording the vaccination in a system such as EHR minimizes the administrative workload as if it were necessary to register the vaccination in a separate solution. That way the data are consolidated with other medical data as well and allow a fractionated healthcare system to ensure, that all physicians and other HCP can retrieve the necessary data on the history, actual situation and provide new information to it.

Therefore, after the administered vaccination is recorded in the vaccination record within the electronic patient management system (e.g., patient's EHR), it is near real-time transferred through the integrated interface to one of the 16 state-level vaccination registries. Through this process, the data are anonymized, without the possibility of re-identification. Hence, the registry contains only anonymized vaccination records. The

reports from the VR (in the following, the central reports) are transmitted to the national level (database at the Robert Koch Institute) in a standardized format.

5.1.1.3 Vaccinations included in the registry

All VRs, except one, include records on all vaccination recommended in the NIP.

Therefore, we would suggest that the STIKO recommendations condition the minimum set of vaccinations contained in the central report. The states can decide independently to collect the data on any additional vaccination.

5.1.1.4 Information on the single vaccination event recorded in the registry

Which information is required to be registered is based on countries requirements regarding the level of individual identification and the extent of use of the VR. The data that would land in the German VRs must be anonymized. Thus, any personal identifiable information such as name, exact address or any personally identification number is not allowed to be collected. For the main scope of the data usage (i.e., VC estimation), anonymised vaccination records suffice.

Person-related information that a single vaccination record must contain is the location of the vaccinee and year of birth. The address which only concerns city and the postal code as seen in Belgium, Walloon and Brussels-Capital Region suffices. Location of the vaccinee can be determined by the location of the GP's office, which he goes to, or with his place of residence. 78.6% of VR collect the information of the location of the vaccinating unit and 71.4% the address of the vaccinee. We do not know which information is used to determine the vaccinee location when estimating the VC. If it is determined with the vaccinating unit, it could still be possible, that the vaccinee lives in one area but goes to the GP's in another. Therefore, we propose to use the postal code of the place of residence of the vaccinee. When a low VC coverage for a specific vaccination or dose is detected, vaccinators can receive feedback for suboptimal VC or missing follow-ups in their area. In Norway, this method was used for the monitoring and follow-up of the 2nd dose of the MMR (35). In this context, the name of the vaccination provider can be collected as well. Contraindications and health insurance status are recorded in only in 2 instances. Therefore, they seem nonessential to be recorded in the

VR. Though recording the contraindications in the patient's EHR can assist the vaccine provider when determining future vaccinations. Recording vaccinee's contact information, such as e-mail or telephone number, which can be used either for recall purposes or follow-up measures, but they should be recorded only in the patient's EHR against his consent.

Information on the vaccination event needed for the VC estimation is (i) date of administration, which is collected in all countries and (ii) vaccine details, such as the name of the product and the batch number. We believe that dose schedule, which is collected in the most countries as well, is necessary to be able to estimate the VC for the second dose of the MMR vaccine, for example.

Majority of the countries record the vaccine batch number (i.e., LOT). That information can be used for vaccine identification as well as the batch- and brand-specific vaccine safety and effectiveness monitoring. The batch number is from the registering point of view a suboptimal choice for vaccine identification since the pre-coded data entry is not feasible, and manual entering allows space for errors. Consequently is the use of barcode readers inevitable and all vaccine provider offices should be therefore equipped with one. This would facilitate the electronic registering of the vaccine information in the patient's EHR as well. At this point not all vaccine manufacturers include the batch number in the barcodes (36). By that means, the EU-Directive 2011/62/EU Delegated Act to protect against falsified medicines (37) could present a step forward. It requires all medicines for human use manufactured, sold or dispensed in the EU including countries like Iceland, Liechtenstein and probably Switzerland, to include GTIN or NTIN (Global/National Trade Item Number), serial number, the national reimbursement number (if requested by Member States), lot/batch number and expiry date in 2D barcode as well as in human readable format until February 2019, in order to be tracked and traced throughout the whole supply chain (from the manufacturing to the dispense) (38).

Importance of the batch number traceability was highlighted in an already mentioned Finnish study, where it was studied whether the onset of narcolepsy was due to a manufacturing error of specific batches of an influenza vaccine since certain batch numbers occurred more frequently in patients who developed narcolepsy (28). In Germany, the anonymization process would disable the re-identification of the individuals vaccinated with the specific batch, but epidemiological studies that do not require the re-identification could still be performed.

Recording of side effects or better, adverse events following immunization (AEFI) can also answer important pharmacovigilance questions, and facilitate HCP's decisions for following vaccinations. In Belgium, Flanders Region, for example, the AEFIs can be recorded and marked in colour, so that they can be seen at the point of future vaccinations (18). The manufacturer information and ATC code are collected in only 28.6% of the VRs, and since the name of the product already provides the necessary information, the collection of those seems non-essential. Side effects (AEFI) are recorded in 35.7% of the VRs, which also appears as non-essential for the collection in the VR, but if recorded in the patient's EHR it could aid the process of AEFI reporting and doctor's decisions for future vaccinations. In the same context, patient's contraindications could be collected.

Thereby, we suggest that the information on a single vaccinating event that the central report should contain are the year of birth and postal code of the place of residence of the vaccinee, date of administration, the name of the product, possibly batch number, and dose schedule.

Other information mentioned, could be optionally recorded in the patient's EHR.

5.1.1.5 Master data sources

We learned that each record for an individual in the registry can be created through the link with the population registry or is generated by the healthcare provider. In the most instances, the master data (placeholder for an individual containing information on age and location) in VR is created through the link with the population registry which should provide accurate denominator estimate. The calculation of the VC estimation is much simplified, and the reports can be produced directly from the VR if the VR already includes the information on the denominator (i.e., information of the total number of individuals living in the area). In the case, where the system can electronically transfer this population data in real-time and can automatically consider the data on new live births, deaths, changes of residence address, it helps to minimise some traditional dominator problems of ghosting and unregistered populations (39).

Thus, one option for a single VR in Germany is (i) when the patient's EHR is created, a placeholder in the VR is created as well, and another, (ii) to link the VR with states'

population registry, which feeds the VR with the denominator information. Thereby, in both cases, the VR includes information on the dominator, which enables generation of vaccine coverage reports, directly from the registry.

We would recommend the first option (*the master data (placeholder for an individual containing information on age and location) in the VR is created simultaneously with the patient's EHR*). We believe that this would provide an accurate denominator and offer a solution if there is no population registry available in the state of the VR.

5.1.1.6 Access to the registry

We neither defined the level of the access, nor did we define if the stakeholders have access to the system or only to the data from it, which makes it difficult to determine to which extend the access to stakeholders is enabled and use the information in deciding who should have access to VR in Germany and to what extent. We can only assume that the health authorities have access to the collected data for the use in monitoring of the VC and NIPs, and the healthcare professionals can register the administered vaccines and have insight in their patient's vaccination history. When tackling what level of access to the VR and its data are to be granted to the stakeholders, it is important to think, what information is needed for them to perform their assigned functions.

Vaccine providers should be able to access the individual's immunisation history; they should be able to register the administered vaccines and correct the entry if it appears to be false. Institutions and authorities involved in the NIP development, vaccination policy should have access to the data, which facilitates the decision-making. To promote the scientific research regarding the vaccine safety and effectiveness, vaccination acceptance, health outcome research the appropriate data should be made available for the research institutes.

Thereby, we propose that registering the vaccinations in a single VR in Germany is conditioned by the access to the patient management software solution in the doctor's office, where vaccinations are electronically recorded. The organization responsible for it should be accountable for the highest quality of the data protection, the quality, maintenance of the data and the appropriate data transfer of the central reports to the

national level. They should also oversee who can access the collected data for purposes of VC estimation and other defined data use at the state level. On the national level, RKI should regularly receive the central reports from registries, so that the VC on a national level can be estimated. Other data needed for other studies, such as vaccine effectiveness studies, could be made available upon request to the organization responsible for it.

When it comes to patient's access to his vaccination history, it becomes more evident. In some countries, a separate web-based solution is offered, for the patients to have to access to their vaccination data. As part of the German E-Health Act, the prerequisites should be fulfilled by the end of the year 2018, so that the data from the EHR could be transferred to an electronic compartment (patient has a sovereignty over the transferred data), to which patients could access with the electronic healthcare card³ outside of the doctor's office (25). They should be able to add the data such as blood sugar measurements diary. *Establishment of such electronic compartment would offer an opportunity, where patients could also see and access their electronic vaccination certificates and possibly enter the vaccinations received outside of the doctor's office (administered abroad, by occupational health physicians, schools etc.) themselves.*

5.1.1.7 Reporting process

*Reporting should be done immediately after the vaccination, as it is also done in the 85.7% of the countries, to minimize the lag time of the data availability in the VR. Consequently, underreporting can be reduced and VR includes timely data on the vaccinated population, which is mainly relevant during emergency situations or outbreaks when the prompt response is necessary (18). For the same reason, the data transfer to the VR should be made without significant delays. Reporting is mandatory in 8 cases. In 6 there can be consequences if the vaccination is not reported, but only 3 have legal options, other include non-payment of the vaccinator and some form of system dysfunction. It is hard to imagine, what the consequences in Germany could be, but we believe, that *only if all vaccination providers are be obligated to report all administered vaccines, the completeness of the data can be achieved.**

³ Provided to every statutory health insured individual.

Evaluation of the comprehensiveness and quality of the data seems an important measure to verify and evaluate the validity, reliability, and completeness of the reported data.

5.1.1.8 *Features of the registry*

Based on the structure we decided, the features of the registry as described in the results in chapter 4.2.2.15, would be assigned to the patient management software's in the doctor's office as it is done in Norway. Such software would assist the doctor with determining the appropriate vaccinations for their patient and with the appointment scheduling.

We learned that one of the most essential and supporting tools for assuring, that individuals receive the recommended vaccinations and do not miss them, is the so-called call-recall system (i.e., production of the letters of invitation for the vaccination and reminder letters for the upcoming or missed vaccinations). Such system could be integrated into the patient management system, and if desired by the vaccinee, they could receive such notifications. Such interventions are widely recognized as a valuable measure to assist the vaccine provider and the vaccinee to acquire appropriate vaccinations (40) (41) (42) (43).

Other features assisting the doctor integrated into the patient management system, that could be included, and are used in some countries, are foreseeing the immunization plan for the patient; recommending the time for the next vaccination appointment and adjusting the dates according to the previous vaccinations.

Only a few countries record reasons for missed vaccination. If reasons for that are due to patient's uncertainties, such features could help the physicians to address patient's concerns appropriately. Through collecting such information, general acceptance of the vaccinations can be researched and help to target these uncertainties with educational campaigns, etc. If the reason is medical, it gives the physician valuable information for planning future vaccinations.

We would propose, that *the vaccination record which is part of patient management system includes call-recall feature upon request of the patient; can foresee of the*

vaccination schedule for a specific age group and includes appointment scheduling assistant.

5.1.1.9 Linkage to other registries

The results showed that no registry is linked to any of other registries or databases, though in some countries it is possible to connect it manually, or the data from different registries can be matched, where the same unique identifier is used (Finland). Thereby, valuable vaccine effectiveness and safety studies can be performed. A connection of the data with the registries holding the information on occurred cases of the VPD can be an excellent tool for vaccine effectiveness assessment. Connecting it with the data from health outcome registers can provide valuable information on vaccine safety and with screening results registry on vaccine effectiveness, e.g., linkage of the VC data with HPV and cervical cancer screening results register can provide information on HPV vaccine effectiveness as well as on the impact of the HPV immunization programme. In Germany, a law (Act to modernize the epidemiological surveillance of communicable diseases) (44) has been introduced recently. Its central regulation creates the basis for an implementation of an electronic reporting and information system for infection control (DEMIS) by the end of 2020. Although the anonymization process would restrict one to one connection of the individual data, this seems an excellent opportunity for data connection, to perform epidemiological studies.

6 CONCLUSION

We identified a questionnaire-based survey as a suitable method to collect information that would support our decision-making when developing a concept of a German VR. However, this approach had some limitations. The questionnaires collected predominantly quantitative information. Therefore, it was hard to determine the weight of the particular information. To achieve high response rate, we had to keep the questionnaires brief, appealing for answering, with as many close-ended questions, and easy to answer with as little by-help as possible. Thus, they were probably in some respects not detailed enough or even not tackling the specific subject at all. This exposed the gaps in information, allowing space for assumptions or may also leave out some points, which should be considered when developing a concept for a VR. Furthermore, pre-suggested answers could be more likely chosen, and the option “Others” could, therefore, be more often omitted. In addition to that, the respondents may understand questions differently as well as we may interpret the answers wrong. Although overall, we believe that we were able to capture many important aspects.

Vaccination registries became vital part of many immunization programmes and eHealth initiatives across Europe. Well-established vaccination registries deliver timely data on VC for the whole population. When gaps in VC (e.g., cohorts, regions) are identified, rapid and target-group specific interventions are possible. Furthermore, the data support the evidence-based vaccination policy making and decisions, immunization programme monitoring and development, monitoring of vaccine effectiveness and safety as well as bring new research opportunities. By providing the consolidated immunization histories and with features such as call-recall system and scheduling assistant, they benefit vaccine providers by assisting them with determining appropriate vaccinations and patients by providing them with necessary and avoiding the unnecessary double vaccinations.

Fragmented health system and strong data protection rules in Germany make a challenging environment for such system, but the exchange of information, knowledge, and shared best practices with countries with established vaccination registries facilitates

its development by offering an opportunity to find common points, identify areas of challenge and addressing them appropriately.

The proposed setting for Germany is a network of 16 vaccination registries in each of the federal state covering their geographic jurisdiction. They should have common functional standards, software and minimum required data to be collected, to increase the interoperability and facilitate the collection of the data on the national level. After the administered vaccination is recorded in the electronic patient management system, it is transferred through the integrated interface to the one of the state-level VR. Through this process, the data are anonymized. Thus, the registry contains anonymized vaccination records. The reports from the VR (in the following, the central report) are near real-time transmitted to the national level in a standardized format. We would recommend that the minimum set of vaccinations contained in the central report should be conditioned by the vaccinations in the STIKO recommendations. The states can, therefore, decide independently to collect the data on any additional vaccination. The information on the single vaccination event that the central report contains is the year of birth and postal code of the place of residence of the vaccinee, the date of the vaccine administration, the name of the product, possibly the batch number and dose schedule. Registering the vaccinations is conditioned by the access to the patient management software solution in the doctor's office, where vaccinations are electronically recorded. The organization owning the VR is responsible for the highest quality of the data protection, the quality, maintenance of the data and the appropriate data transfer of the central reports to the national level. They would also oversee who can access the collected data for purpose of VC estimation and other defined data use at the state level. On the national level, the RKI receives the central reports from registries, so that the VC can be estimated on the national level. Other data needed for other studies, e.g. vaccine effectiveness studies, could be made available upon request to the responsible organization. The vaccinee would access his electronic vaccination records in the electronic patient compartment. Reporting of the vaccinations and data transfer from the registering system to the VR must be done immediately, to minimize the lag time of the data availability in the VR. The data reported should be evaluated for completeness and its quality. Call-recall system feature, the foresight of the vaccination schedule for a specific age group and appointment scheduling assistant were identified as being the most valuable, therefore we

propose that the patient management systems where the vaccinations are registered have these features integrated.

Implementation of a VR in Germany would be a step forward towards the modernization and improvement of the vaccination process and health informatics, benefiting the vaccine providers, vaccinated individuals, decision-makers, and research institutions. It would bring a better and more comprehensive overview of VC and could serve as a single source of data for vaccine coverage estimation and fill the information and timeliness gaps in the data collected with the current methods.

7 REFERENCES

1. Zhou F, Shefer A, Wenger J, Messonnier M, Wang LY, Lopez A, Moore M, V. Murphy T, Cortese M, Rodewald L. Economic Evaluation of the Routine Childhood Immunization Program in the United States, 2009. *Pediatrics*, 2014, Vol. 133(4), pp. 577-585.
2. European Centre for Disease Prevention and Control, Infectious diseases & public health. Table. Number of measles cases by month and notification rate (cases per million) by country, January 2015 to December 2015, EU/EEA countries. [Online] 31 December 2015. [Cited: 03 December 2017.] <https://ecdc.europa.eu/en/publications-data/table-number-measles-cases-month-and-notification-rate-cases-million-country-11>.
3. European Centre for Disease Prevention and Control, Infectious diseases & public health. Table. Number of measles cases by month and notification rate (cases per million) by country, January 2016 to December 2016, EU/EEA countries. [Online] 26 January 2017. [Cited: 03 December 2017.] <https://ecdc.europa.eu/en/publications-data/table-number-measles-cases-month-and-notification-rate-cases-million-country>.
4. WHO Regional Office for Europe. Immunization highlights: European Vaccine Action Plan progress report for 2016. [Online] [Cited: 5 November 2017.] <http://www.euro.who.int/en/health-topics/disease-prevention/vaccines-and-immunization/publications/2017/immunization-highlights-european-vaccine-action-plan-progress-report-for-2016>.
5. Fine P, Eames K, L. Heymann D. “Herd Immunity”: A Rough Guide. *Clinical Infectious Diseases*, 2011, Vol. 52(7), pp. 911-916.
6. Burton A, Monasch R, Lautenbach B, Gacic-Dobo M, Neill M, Karimov R, Wolfson L, Jones G, Birmingham M. WHO and UNICEF estimates of national infant immunization coverage: methods and processes. *Bulletin of the World Health Organization*., 2009, Vol. 87, pp. 535-541.
7. World Health Organization, WHO. Immunization coverage. [Online] 2017. [Cited: 19 November 2017.] http://www.who.int/immunization/monitoring_surveillance/routine/coverage/en/.
8. Laroche JA, Diniz AJ. Immunisation registers in Canada: progress made, current situation, and challenges for the future. *Eurosurveillance*, 2012, Vol. 17(17), pp. 17-22.
9. Siedler A, Rieck T, Reuss A, Walter D, Poggensee G, Poethko-Müller C, Reiter S. Estimating vaccination coverage in the absence of immunisation registers – the German experience. *Eurosurveillance*, 2012, Vol. 17(17), pp. 23-29.
10. Gesetz zur Verhütung und Bekämpfung von Infektionskrankheiten beim Menschen (Infektionsschutzgesetz - IfSG) (Infection Protection Act). 2000, *Bundesgesetzblatt (BGBl) I*, 2000, pp. 1045.
11. Rieck T, Feig M, an der Heiden M, Siedler A, Wichmann O. Assessing varicella vaccine effectiveness and its influencing factors using health insurance claims data, Germany, 2006 to 2015. *Eurosurveillance*, 2017, Vol. 22(17), pp. 21-30.

12. Centres for Disease Control and Prevention. Immunization Information Systems. About Immunization Information Systems. [Online] 15 May 2012. [Cited: 24 November 2017.] <https://www.cdc.gov/vaccines/programs/iis/about.html>.
13. Trogstad L, Ung G, Hagerup-Jenssen M, Cappelen I, Haugen IL, Feiring B. The Norwegian immunisation register – SYSVAK. *Eurosurveillance*, 2012, Vol. 17(16), pp. 11-17.
14. Vaccine European New Integrated Collaboration Effort project, VENICE. Survey on Functional Standards for Computerised Immunisation Registries in Europe, 2008. [Online] 12 June 2010. [Cited: 05 November 2017.] http://venice.cineca.org/Final_Report_Functional_Standards_v1.0_.pdf.
15. Bernal-González PJ, Navarro-Alonso JA, Pérez-Martín JJ. Computerised vaccination register for the Murcia region, Spain, 1991 to 2011. *Eurosurveillance*, 2012, Vol. 17(16), pp. 18-23.
16. Aguilar I, Reyes M, Martínez-Baz I, Guevara M, Albéniz E, Belza MJ, Castilla J. Use of the vaccination register to evaluate influenza vaccine coverage in seniors in the 2010/11 influenza season, Navarre, Spain. *Eurosurveillance*, 2012, Vol. 17(17), pp. 36-41.
17. Johansen K, Lopalco PL, Giesecke J. Immunisation registers – important for vaccinated individuals, vaccinators and public health. *Eurosurveillance*, 2012, Vol. 17(16), pp. 2-4.
18. Derrough T, Olsson K, Gianfredi V, Simondon F, Heijbel H, Danielsson N, Kramarz P, Pastore-Celentano L. Immunisation Information Systems – useful tools for monitoring vaccination programmes in EU/EEA countries, 2016. *Eurosurveillance*, 2017, Vol. 22(17), pp. 10-20.
19. Crowcroft NS, Levy-Bruhl D. Registries: An essential tool for maximising the health benefits of immunisation in the 21st century. *Eurosurveillance*, 2017, Vol. 22(17), pp. 2-4.
20. Council of the European Union. Council conclusions on childhood immunisation: successes and challenges of European childhood immunisation and the way forward invites. [Online] 08 July 2011. [Cited: 24 November 2017.] Available online: http://eur-lex.europa.eu/legal-content/EN/ALL/?uri=uriserv:OJ.C_.2011.202.01.0004.01.ENG.
21. IQWiG (Institute for Quality and Efficiency in Health Care). Health care in Germany: The German health care system. *Informed Health Online* [Internet], 2015. [Cited: January 2 2018.] <https://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0078021/>
22. Oppermann H, Wahl G, Borrmann M, Fleischer J. Impfmeldepflicht in Sachsen-Anhalt Möglichkeiten und Grenzen der Entwicklung eines elektronischen Impfregisters. *Bundesgesundheitsblatt*, 2009, Issue 52, pp. 1029–1036.
23. Die Bundesbeauftragte für den Datenschutz und die Informationsfreiheit. Bundesdatenschutzgesetz - Text und Erläuterungen. [Online] December 2017. [Cited: 05 November 2017.] <https://www.bfdi.bund.de/SharedDocs/Publikationen/Infobroschueren/INFO1.html>.
24. European Commission. European Commission Justice. Reform of EU data protection rules. [Online] [Cited: 25 November 2017.] http://ec.europa.eu/justice/data-protection/reform/index_en.htm.
25. Bundesgesundheitsministerium. E-Health Gesetz - Bundesgesundheitsministerium. [Online] [Cited: 15 December 2017.] www.bundesgesundheitsministerium.de/service/begriffe-von-a-z/e/e-health-gesetz.html.

26. Gesundheitsministerkonferenz (GMK). Beschlüsse der 89. GMK (2016), TOP: 7.6 Nationales Impfreister für Deutschland. [Online] [Cited: 05 November 2017.] <https://www.gmkonline.de/Beschluesse.html?id=432&jahr=2016>.
27. Guzmán Herrador BR, Aavitsland P, Feiring B, A Riise Bergsaker M, Borgen K. Usefulness of health registries when estimating vaccine effectiveness during the influenza A(H1N1)pdm09 pandemic in Norway. *BMC Infectious Diseases*, 2012, Vol. 12(63). Available online: <https://bmcinfectdis.biomedcentral.com/articles/10.1186/1471-2334-12-63>
28. Nohynek H, Jokinen J, Partinen M, Vaarala O, Kirjavainen T, Sundman J, et al. AS03 adjuvanted AH1N1 vaccine associated with an abrupt increase in the incidence of childhood narcolepsy in Finland. *PLoS ONE*, 2012, Vol. 7(3), pp. 335-336.
29. Arnheim-Dahlström L, Pasternak B, Svanström H, Sparén P, Hviid A. Autoimmune, neurological, and venous thromboembolic adverse events after immunisation of adolescent girls with quadrivalent human papillomavirus vaccine in Denmark and Sweden: cohort study. *BMJ*, 2013, Vol. 347, pp. f5906.
30. A van Lier, P Oomen, P de Hoogh, I Dr fhout, B Elsinghorst, J Kemmeren, M Conyn-van Spaendonck, H de Melker. Præventis, the immunisation register of the Netherlands: a tool to evaluate the National Immunisation Programme. *Eurosurveillance*, 2012, Vol. 17(17), pp. 11-16.
31. Wilson SE, Quach S, MacDonald SE, Naus M, Deeks SL, Crowcroft NS, Mahmud SM, Tran D, Kwong JC, Tu K, Johnson C, Desai S. Immunization information systems in Canada: Attributes, functionality, strengths and challenges. A Canadian Immunization Research Network study. *Can J Public Health*, 2012, Vol. 107(6), pp. e575–e582.
32. GOV.UK. Public Health England. COVER vaccine coverage data submission forms. Document: Immunisation data: parameters for quarterly data submission (October to December 2017) [Online] [Cited: 25 November 2017.] <https://www.gov.uk/government/publications/immunisation-data-what-to-submit-when>
33. Alfonsi V, D’Ancona F, Rota MC, Giambi C, Ranghiasi A, Iannazzo S. Immunisation registers in Italy: a patchwork of computerisation. *Eurosurveillance*, 2012, Vol. 17(17), pp. 30-35.
34. Statens Serum Institute. EPI-NEWS: The first year with statutory registration of vaccinations in the Danish Vaccination Register. [Online] 2016 November 09. [Cited: 03 December 2017.] <https://www.ssi.dk/English/News/EPI-NEWS/2016/No%2045%20-%202016.aspx>.
35. Hagerup-Jenssen M, Kongsrud S, Riise ØR. Suboptimal MMR2 vaccine coverage in six counties in Norway detected through the national immunisation registry, April 2014 to April 2017. *Eurosurveillance*, 2017, Vol. 22(17), pp. 39-44.
36. Baum U, Sundman J, Jääskeläinen S, Nohynek H, Puumalainen T, Jokinen J. Establishing and maintaining the National Vaccination Register in Finland. *Eurosurveillance*, 2017, Vol. 22(17), pp. 45-53.
37. The European Parliament and the Council. Directive 2011/62/EU of the European Parliament and of the Council of 8 June 2011 amending Directive 2001/83/EC on the Community code relating to

medicinal products for human use, as regards the prevention of the entry into the legal supply chain of falsified medicinal products (Text with EEA relevance). Official Journal of the European Union, 2011, Issue 174, pp. 74-87.

38. European Commission. Medicinal products for human use, Falsified medicines. [Online] [Cited: 03 December 2017.] https://ec.europa.eu/health/human-use/falsified_medicines_en#geninf.

39. Pebody, R. Vaccine registers – experiences from Europe and elsewhere. *Eurosurveillance*, 2012, Vol. 17 (17), pp. 2-4.

40. CH Suppli, M Rasmussen, P Valentiner-Branth, K Mølbak, TG Kraus. Written reminders increase vaccine coverage in Danish children - evaluation of a nationwide intervention using e Danish Vaccination Register, 2014 to 2015. *Eurosurveillance*, 2017, Vol. 22(17), pp. 31-37.

41. Jacobson Vann JC, Szilagy P. Patient reminder and patient recall systems to improve immunization rates. *Cochrane Database Systematic Reviews*, 2005, Vol. 3.

42. Harvey H, Reissland N, Mason J. Parental reminder, recall and educational interventions to improve early childhood immunisation uptake: A systematic review and meta-analysis. *Vaccine*, 2015, Vol. 30 (25), pp. 2862-80.

43. Kharbanda EO, Stockwell MS, Fox HW, Andres R, Lara M, Rickert VI. Text message reminders to promote human papillomavirus vaccination. *Vaccine*, 2011, Vol. 29, pp. 2537-41.

44. Gesetz zur Modernisierung der epidemiologischen Überwachung übertragbarer Krankheiten (Act to modernize the epidemiological surveillance of communicable diseases). *Bundesgesetzblatt (BGBl) II Nr. 49*, 2017, pp. 2615-2639.

8 APPENDICES

Appendix 1: Invitation for the survey and research questionnaires

To whom it may concern,

My name is Petra Srdič, and I am a student at the University of Ljubljana, Faculty of Pharmacy. I am doing research for my master thesis. My mentor is Mitja Kos, Associate Professor and Head of the Chair of Social Pharmacy at Faculty of Pharmacy. I am currently doing a traineeship in a pharmaceutical company in Germany, where I deepened my interest and knowledge about vaccines and their importance for public health. I believe that a system for complete recording of vaccinations is of great help for health authorities to evaluate and supervise the vaccination situation in the country and consequently, most importantly, by raising the vaccination coverage it benefits public health in great extent. And this is the topic I am addressing in my master thesis.

The objective of my master thesis research is to examine possibilities of implementation a vaccination registry in Germany and develop a proposal for one. Because I would like to learn from experiences of other countries with such systems, I am now turning to you. **I would be very grateful if you could take some time, to read this e-mail and take time to answer the questionnaire I prepared for you.**

I would define vaccination registry as any national, regional or local electronic, computerized system, registry or database, capturing data on administered vaccines to individuals.

To collect the relevant data for my research on existing vaccination registries in European countries I designed two questionnaires. Which one is relevant for you, depends whether a vaccination registry in your country exist or it does not. Because the questionnaire *Vaccination registry is in place* contains detailed questions on vaccination registry, I would kindly ask you, to either provide me with the contact of the organization responsible for it or forward this e-mail to the relevant contact and carbon copy me, if that is applicable for you. If there are more vaccination registries on a local or regional level, I would kindly ask you to provide me with contacts, responsible for them.

This questionnaire is an important part of my data collection methodology, which is why I would appreciate your support a lot. The questionnaires are consisting of open- and close-ended arrangements and it should not take more than 15 minutes to answer.

I guarantee that all information will be used only for this research.

I hope you will be willing to respond to me and help me to learn from your case.
A prompt response would be much appreciated.

Yours Sincerely,

Petra Srdič

Questionnaire 1: Vaccination registry is in place

Name and surname:

Name of the organization:

Name of the vaccination registry:

I. What is your country's healthcare structure?

- Centralized
 Decentralized

II. Which vaccinations are recommended in the national immunization programme (NIP)

- | | |
|---|--|
| <input type="checkbox"/> Diphtheria | <input type="checkbox"/> Mumps |
| <input type="checkbox"/> Haemophilus influenza type b | <input type="checkbox"/> Pertussis |
| <input type="checkbox"/> Hepatitis A | <input type="checkbox"/> Pneumococcal disease |
| <input type="checkbox"/> Hepatitis B | <input type="checkbox"/> Poliomyelitis |
| <input type="checkbox"/> Herpes zoster (shingles) | <input type="checkbox"/> Rabies |
| <input type="checkbox"/> Human papillomavirus | <input type="checkbox"/> Rotavirus gastroenteritis |
| <input type="checkbox"/> Influenza | <input type="checkbox"/> Rubella |
| <input type="checkbox"/> Japanese encephalitis | <input type="checkbox"/> Tetanus |
| <input type="checkbox"/> Measles | <input type="checkbox"/> Tick-borne encephalitis |
| <input type="checkbox"/> Meningococcal disease serogroups A, C, W135, Y | <input type="checkbox"/> Typhoid fever |
| <input type="checkbox"/> Meningococcal disease serogroup C | <input type="checkbox"/> Varicella |
| <input type="checkbox"/> Meningococcal disease serogroup B | <input type="checkbox"/> Yellow fever |

III. Are vaccinations in your country voluntary or compulsory?

- Fully voluntary (if chosen, please go to next question)
 Compulsory (if chosen, please answer the section a.)

a. Vaccinations against which diseases are compulsory?

- | | |
|---|--|
| <input type="checkbox"/> Diphtheria | <input type="checkbox"/> Mumps |
| <input type="checkbox"/> Haemophilus influenza type b | <input type="checkbox"/> Pertussis |
| <input type="checkbox"/> Hepatitis A | <input type="checkbox"/> Pneumococcal disease |
| <input type="checkbox"/> Hepatitis B | <input type="checkbox"/> Poliomyelitis |
| <input type="checkbox"/> Herpes zoster (shingles) | <input type="checkbox"/> Rabies |
| <input type="checkbox"/> Human papillomavirus | <input type="checkbox"/> Rotavirus gastroenteritis |
| <input type="checkbox"/> Influenza | <input type="checkbox"/> Rubella |
| <input type="checkbox"/> Japanese encephalitis | <input type="checkbox"/> Tetanus |
| <input type="checkbox"/> Measles | <input type="checkbox"/> Tick-borne encephalitis |
| <input type="checkbox"/> Meningococcal disease serogroups A, C, W135, Y | <input type="checkbox"/> Typhoid fever |
| <input type="checkbox"/> Meningococcal disease serogroup C | <input type="checkbox"/> Varicella |
| <input type="checkbox"/> Meningococcal disease serogroup B | <input type="checkbox"/> Yellow fever |

IV. Are vaccinations in your country reimbursed?

- Yes, fully reimbursed (if chosen, please answer the section a.)
- Yes, partially reimbursed (if chosen, please answer the section a.)
- No, there is no reimbursement (if chosen, please go to next question)

a. Vaccinations against which diseases are partially or fully reimbursed?

- | | |
|---|--|
| <input type="checkbox"/> Diphtheria | <input type="checkbox"/> Mumps |
| <input type="checkbox"/> Haemophilus influenza type b | <input type="checkbox"/> Pertussis |
| <input type="checkbox"/> Hepatitis A | <input type="checkbox"/> Pneumococcal disease |
| <input type="checkbox"/> Hepatitis B | <input type="checkbox"/> Poliomyelitis |
| <input type="checkbox"/> Herpes zoster (shingles) | <input type="checkbox"/> Rabies |
| <input type="checkbox"/> Human papillomavirus | <input type="checkbox"/> Rotavirus gastroenteritis |
| <input type="checkbox"/> Influenza | <input type="checkbox"/> Rubella |
| <input type="checkbox"/> Japanese encephalitis | <input type="checkbox"/> Tetanus |
| <input type="checkbox"/> Measles | <input type="checkbox"/> Tick-borne encephalitis |
| <input type="checkbox"/> Meningococcal disease serogroups A, C, W135, Y | <input type="checkbox"/> Typhoid fever |
| <input type="checkbox"/> Meningococcal disease serogroup C | <input type="checkbox"/> Varicella |
| <input type="checkbox"/> Meningococcal disease serogroup B | <input type="checkbox"/> Yellow fever |

V. General information about the vaccination registry

What year was it implemented?

Who is responsible for it?

VI. Vaccinations and information recorded in the vaccination registry:

What is the information level available?

National (if chosen, please go to next question)

Regional (if chosen, please answer the section a. and b.)

Local (if chosen, please answer the section a. and b.)

a. Are there common standards and requirements for the regional/local vaccination registries?

Yes

No

b. Is it challenging to obtain data on the national level?

No

Yes

If yes, what are the challenges you are facing?

Vaccinations against which diseases are included in the vaccination registry?

Diphtheria

Haemophilus influenza type b

Hepatitis A

Hepatitis B

Herpes zoster (shingles)

Human papillomavirus

Influenza

Japanese encephalitis

Measles

Meningococcal disease serogroups A, C, W135, Y

Meningococcal disease serogroup C

Mumps

Pertussis

Pneumococcal disease

Poliomyelitis

Rabies

Rotavirus gastroenteritis

Rubella

Tetanus

Tick-borne encephalitis

Typhoid fever

Varicella

Meningococcal disease serogroup B

Yellow fever

Which information on the vaccination is included in vaccination registry?

Date of administration of the vaccine

Name of the vaccinator

Name and location of the vaccinating unit (of e.g. health clinic, general practice)

Product name

Batch number

Manufacturer

Dose schedule (primary, booster series)

ATC code

Side effects, if occurred

Others:

How is the master data of the vaccination registry generated?

Automatically through data transfer from population registry

By payers

By health care provider

Other:

Which information on the vaccinee is included?

Name

Date of birth

Address

Contact (e.g. e-mail, telephone number)

Health insurance status (Health insurance company)

Contraindications

Identification number

Others:

VII. Access to the vaccination registry

Who can access to the vaccination registry?

- Ministry of Health and other authorities
- Payer
- Physicians (E.g. General practitioners)
- Nurse
- Patient
 - Access to his vaccination record
 - Other:
- Others:

VIII. Reporting to the vaccination registry

Is reporting to the system mandatory?

- Yes (if chosen, please answer the section a.)
- No (if chosen, please go to next question)

a. What are the consequences if vaccination is not reported?

Should each vaccination be reported immediately?

- Yes
- No

Is an evaluation made on comprehensiveness and quality of reporting?

- Yes
- No

IX. Vaccination coverage

Are there any other means used to calculate vaccination coverage?

- Yes (if chosen, please answer the section a.)
- No

a. What are other methods used?

- Population surveys
- School entry examinations
- Health insurance refund claim data

Other:

Is it possible to identify cohorts with poor vaccination coverage?

Yes No

Is it possible to identify regions with poor vaccination coverage?

Yes No

Is it possible to calculate vaccination coverage for any chosen parameter? (E.g. age, gender, region ...)

Yes (if chosen, please answer section a.) No (if chosen, please go to next question)

a. *For which parameters?*

X. Other uses of the data obtained from vaccination registry (more than one answer possible):

Developing of national immunization recommendations or programmes (E.g. for specific age groups, predicting outbreaks...)

Evaluating the effectiveness and impact of a national immunization programme

Monitoring the effectiveness and safety of the vaccines

Evaluating the effectiveness and impact of a national immunization programme

Research purposes

Recruiting of the individuals included in the vaccination registry for further research

Other:

XI. What features has the system? (more than one answer possible)

- Producing letters of invitation for the national immunization programme
- Producing reminder letters
- Managing vaccination appointments
- Foreseeing the vaccination plan in the system
- Capability of adjusting the dates if vaccination is given too late
- Registering information on reasons for missed vaccinations
- Managing vaccine stock
- Others:

XII. Is the vaccine register linked to any other register? (more than one answer possible)

- Screening results registers
Which ones?
- Health outcome registers
Which ones?
- Others:

XIII. Supplemental information

What was the impact of the implementation of the vaccination registry?

- a. Vaccination against measles
 - Increased vaccination coverage (VC)
 - Unchanged VC
 - Decreased VC

- b. Vaccination against mumps
 - Increased VC
 - Unchanged VC
 - Decreased VC

c. Vaccination against rubella

Increased VC

Unchanged VC

Decreased VC

d. Vaccination against pertussis

Increased VC

Unchanged VC

Decreased VC

e. Vaccination against varicella

Increased VC

Unchanged VC

Decreased VC

Is there any literature regarding your vaccination registry that can be shared with us?

Is there any other important information that you can share with us to help us understand your vaccination registry?

Thank you for your time!

Questionnaire 2: Vaccination registry is not in place

Name and surname:

Name of the organization:

XIV. What is your country's health structure?

- Centralized
- Decentralized

XV. Which vaccinations are recommended in the national immunization program (NIP)

- | | |
|---|--|
| <input type="checkbox"/> Diphtheria | <input type="checkbox"/> Mumps |
| <input type="checkbox"/> Haemophilus influenza type b | <input type="checkbox"/> Pertussis |
| <input type="checkbox"/> Hepatitis A | <input type="checkbox"/> Pneumococcal disease |
| <input type="checkbox"/> Hepatitis B | <input type="checkbox"/> Poliomyelitis |
| <input type="checkbox"/> Herpes zoster (shingles) | <input type="checkbox"/> Rabies |
| <input type="checkbox"/> Human papillomavirus | <input type="checkbox"/> Rotavirus gastroenteritis |
| <input type="checkbox"/> Influenza | <input type="checkbox"/> Rubella |
| <input type="checkbox"/> Japanese encephalitis | <input type="checkbox"/> Tetanus |
| <input type="checkbox"/> Measles | <input type="checkbox"/> Tick-borne encephalitis |
| <input type="checkbox"/> Meningococcal disease serogroups A, C, W135, Y | <input type="checkbox"/> Typhoid fever |
| <input type="checkbox"/> Meningococcal disease serogroup C | <input type="checkbox"/> Varicella |
| <input type="checkbox"/> Meningococcal disease serogroup B | <input type="checkbox"/> Yellow fever |

XVI. Are vaccinations in your country voluntary or compulsory?

- Fully voluntary (if chosen, please go to next question)
- Compulsory (if chosen, please answer the section a.)

b. Vaccinations against which diseases are compulsory?

- | | |
|---|--|
| <input type="checkbox"/> Diphtheria | <input type="checkbox"/> Mumps |
| <input type="checkbox"/> Haemophilus influenza type b | <input type="checkbox"/> Pertussis |
| <input type="checkbox"/> Hepatitis A | <input type="checkbox"/> Pneumococcal disease |
| <input type="checkbox"/> Hepatitis B | <input type="checkbox"/> Poliomyelitis |
| <input type="checkbox"/> Herpes zoster (shingles) | <input type="checkbox"/> Rabies |
| <input type="checkbox"/> Human papillomavirus | <input type="checkbox"/> Rotavirus gastroenteritis |
| <input type="checkbox"/> Influenza | <input type="checkbox"/> Rubella |
| <input type="checkbox"/> Japanese encephalitis | <input type="checkbox"/> Tetanus |
| <input type="checkbox"/> Measles | <input type="checkbox"/> Tick-borne encephalitis |
| <input type="checkbox"/> Meningococcal disease serogroups A, C, W135, Y | <input type="checkbox"/> Typhoid fever |
| <input type="checkbox"/> Meningococcal disease serogroup C | <input type="checkbox"/> Varicella |
| <input type="checkbox"/> Meningococcal disease serogroup B | <input type="checkbox"/> Yellow fever |

XVII. Are vaccinations in your country reimbursed?

- Yes, fully reimbursed (if chosen, please answer the section a.)
- Yes, partially reimbursed (if chosen, please answer the section a.)
- No, there is no reimbursement (if chosen, please go to next question)

b. Vaccinations against which diseases are partially or fully reimbursed?

- | | |
|---|--|
| <input type="checkbox"/> Diphtheria | <input type="checkbox"/> Mumps |
| <input type="checkbox"/> Haemophilus influenza type b | <input type="checkbox"/> Pertussis |
| <input type="checkbox"/> Hepatitis A | <input type="checkbox"/> Pneumococcal disease |
| <input type="checkbox"/> Hepatitis B | <input type="checkbox"/> Poliomyelitis |
| <input type="checkbox"/> Herpes zoster (shingles) | <input type="checkbox"/> Rabies |
| <input type="checkbox"/> Human papillomavirus | <input type="checkbox"/> Rotavirus gastroenteritis |
| <input type="checkbox"/> Influenza | <input type="checkbox"/> Rubella |
| <input type="checkbox"/> Japanese encephalitis | <input type="checkbox"/> Tetanus |
| <input type="checkbox"/> Measles | <input type="checkbox"/> Tick-borne encephalitis |
| <input type="checkbox"/> Meningococcal disease serogroups A, C, W135, Y | <input type="checkbox"/> Typhoid fever |
| <input type="checkbox"/> Meningococcal disease serogroup C | <input type="checkbox"/> Varicella |
| <input type="checkbox"/> Meningococcal disease serogroup B | <input type="checkbox"/> Yellow fever |

XVIII. Immunization databases

Are there any other databases for recording administered vaccines or recording immunization status available in your country?

Yes (if chosen, please answer the section a.)

Which ones?

Health care claim data

Other:

No, administered vaccines are only recorded in patient's paper / electronic / paper and electronic immunization record (if chosen, please answer the section a.)

No, administered vaccines are not recorded (if chosen, please go to next question)

a. Are the vaccination data reported representative for the whole population?

Yes

No

XIX. How is the vaccination coverage calculated in your country? (more than one answer possible)

Population surveys

School entry examinations

Health insurance claim data

Other:

What are limitations of your approach of calculating vaccination coverage?

XX. Can regions with poor vaccination coverage be identified?

Yes

No

XXI. Can cohorts with poor vaccination coverage be identified?

Yes

No

XXII. What is the limiting factor for not having register in your country? (more answers possible)

Governance concerns

Budget concerns

IT infrastructure not in place

Decentralized health system

Data confidentiality concerns

Other:

XXIII. Do you think a vaccination register would be helpful for raising the vaccination coverage in your country?

Yes, because

No, because

XXIV. Is the vaccination registry in development?

Yes

No

Thank you for your time!

Appendix 2: Vaccinations recommended in the national immunization programme in responding countries.

	Diphtheria	Hib	Hepatitis A	Hepatitis B	HPV	Influenza	JE	Measles	MenACWY	MenC	MenB	Mumps	Pertussis	PC	Poliomyelitis	Rabies	Rotavirus	Rubella	Shingles	Tetanus	TBE	Typhus	Varicella	Yellow fever
BE-VLG	●	●		●	●			●		●		●	●	●	●		●	●		●				
BE-WAL, BE-BRU	●	●		●	●	●		●		●		●	●	●	●		●	●		●				
Bulgaria	●	●		●				●				●	●	●	●			●		●				
Switzerland	●	●		●	●	●		●		●		●	●	●	●			●		●	●		●	
Germany	●	●		●	●	●		●		●		●	●	●	●		●	●		●			●	
Denmark	●	●			●			●				●	●	●	●			●		●				
Estonia	●	●		●	●			●				●	●		●		●	●		●				
Finland	●	●			●	●		●				●	●	●	●		●	●		●				
France	●	●		●	●	●		●		●		●	●	●	●			●	●	●				
Wales	●	●			●	●		●	●		●	●	●	●	●		●	●	●	●				
Ireland	●	●		●	●			●		●	●	●	●	●	●		●	●		●				
Iceland	●	●			●	●		●		●		●	●	●	●			●		●				
Italy	●	●		●	●	●		●	●	●	●	●	●	●	●		●		●	●			●	
Liechtenstein	●	●		●	●	●		●		●		●	●	●	●					●			●	
Malta	●	●		●	●	●		●				●	●		●			●		●				
the Netherlands	●	●		●	●			●		●		●	●	●	●			●		●				
Norway	●	●			●			●				●	●	●	●		●	●		●				
Portugal	●	●		●	●			●		●		●	●	●	●			●		●				
Sweden	●	●			●			●				●	●	●	●			●		●				
Slovenia	●	●		●	●			●		●		●	●	●	●			●		●				
Slovakia	●	●	●	●	●	●		●	●	●	●	●	●	●	●	●	●	●			●			

BE-VLG: Belgium, Flemish Region, BE-WAL and BE-BRU: Belgium, Walloon and Brussels-Capital Region, Hib: Haemophilus influenzae type B, HPV: Human papillomavirus, JE: Japanese encephalitis, MenACWY: Meningococcal disease serogroups A, C, W135, Y, MenC: Meningococcal disease serogroup C, MenB: Meningococcal disease serogroup B, PC: Pneumococcal disease, TBE: Tick-borne encephalitis.

Appendix 3: Compulsory vaccinations in responding countries, where there is one or more compulsory vaccination.

	Diphtheria	Hib	Hepatitis A	Hepatitis B	HPV	Influenza	JE	Measles	MenACWY	MenC	MenB	Mumps	Pertussis	PC	Poliomyelitis	Rabies	Rotavirus	Rubella	Shingles	Tetanus	TBE	Typhus	Varicella	Yellow fever
BE-VLG															•									
BE-WAL, BE-BRU															•									
Bulgaria	•	•		•					•				•	•	•	•					•		•	
France	•															•					•			
Italy	•			•												•					•			
Malta	•															•					•		•	
Slovenia	•	•		•					•				•	•	•	•					•		•	
Slovakia	•	•		•					•				•	•		•					•		•	

BE-VLG: Belgium, Flemish Region, BE-WAL and BE-BRU: Belgium, Walloon and Brussels-Capital Region, Hib: Haemophilus influenzae type B, HPV: Human papillomavirus, JE: Japanese encephalitis, MenACWY: Meningococcal disease serogroups A, C, W135, Y, MenC: Meningococcal disease serogroup C, MenB: Meningococcal disease serogroup B, PC: Pneumococcal disease, TBE: Tick-borne encephalitis.

Appendix 4: Reimbursed vaccinations in responding countries.

	Diphtheria	Hib	Hepatitis A	Hepatitis B	HPV	Influenza	JE	Measles	MenACWY	MenC	MenB	Mumps	Pertussis	PC	Poliomyelitis	Rabies	Rotavirus	Rubella	Shingles	Tetanus	TBE	Typhus	Varicella	Yellow fever
BE-VLG	•	•		•	•			•		•		•	•	•	•		•	•		•				
BE-WAL, BE-BRU	•	•		•	•			•		•		•	•	•	•			•		•				
Bulgaria	•	•		•				•				•	•	•	•			•		•				
Switzerland	•	•		•	•	•		•		•		•	•	•	•			•		•	•			
Germany	•	•		•	•	•		•		•		•	•	•	•		•	•		•			•	
Denmark	•	•			•			•				•	•	•	•			•		•				
Estonia	•	•		•	•			•				•	•		•		•	•		•				
Finland	•	•			•	•		•				•	•	•	•		•	•		•				
France	•	•		•	•	•		•		•		•	•	•	•			•	•	•				
Wales	•	•			•	•		•	•		•	•	•	•	•		•	•	•	•				
Ireland	•	•		•	•			•		•	•	•	•	•	•		•	•		•				
Iceland	•	•			•	•		•		•		•	•	•	•			•		•				
Italy	•	•		•	•	•		•	•	•	•	•	•	•	•		•	•	•	•			•	
Liechtenstein	•	•		•	•	•		•		•		•	•	•	•			•		•			•	
Malta	•	•		•	•	•		•				•	•		•			•		•				
the Netherlands																								
Norway	•	•			•			•				•	•	•	•		•	•		•				
Portugal																								
Sweden	•	•			•			•				•	•	•	•			•		•				
Slovenia	•	•		•	•			•				•	•	•	•	•		•		•				
Slovakia	•	•	•	•	•	•		•		•	•	•	•	•	•	•		•		•				

BE-VLG: Belgium, Flemish Region, BE-WAL and BE-BRU: Belgium, Walloon and Brussels-Capital Region, Hib: Haemophilus influenzae type B, HPV: Human papillomavirus, JE: Japanese encephalitis, MenACWY: Meningococcal disease serogroups A, C, W135, Y, MenC: Meningococcal disease serogroup C, MenB: Meningococcal disease serogroup B, PC: Pneumococcal disease, TBE: Tick-borne encephalitis.