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RiskAware TTS - Protocol

Impact of EU label changes and regulatory communication on SARS-CoV-2 adenovirus vector vaccines in context of thrombosis with thrombocytopenia syndrome (TTS): risk awareness and adherence

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1. Aims of the project

The European Medicines Agency (EMA) has provided recommendations in 2021 to learned societies and healthcare professionals when assessing people with signs and symptoms of thrombosis with thrombocytopenia syndrome (TTS) after being vaccinated with adenovirus vector vaccines Vaxzevria or COVID-19 Vaccine Janssen.
In addition, the EMA also published safety updates on these vaccines, highlights from expert meetings and news items on its website.

This study aims to evaluate the impact of the regulatory actions for Vaxzevria and for COVID-19 Vaccine Janssen following the 2021 review. In this context, the impact of regulatory actions means looking into:

- Whether national COVID-19 vaccination policies were altered following the regulatory actions.
- Whether healthcare professionals are aware and know about the risk of thrombosis with thrombocytopenia syndrome when administering these vaccines.
- Whether attitudes of healthcare professionals and public have changed towards national COVID-19 vaccination programmes after the 2021 recommendations.

The study's objectives are:

1. To determine the extent of how regulatory actions for thrombosis with thrombocytopenia syndrome (TTS) have changed **national vaccination policy**, including change in risk and age group prioritization, change in recommendations for the second vaccine dose and recommendations for other SARS-CoV-2 vaccines available at the time, by country, and by vaccine brand.

2. To determine the level of **healthcare professional awareness** and knowledge of the risk of TTS and their adherence to Summary of Product Characteristics (SmPC) recommendations for SARS-CoV-2 adenovirus vector vaccines, with particular focus on the following elements:
    2.1. Receipt and awareness of the direct healthcare professional communications (DHPC).
    2.2. Knowledge and awareness of the signs and symptoms of TTS and the need for healthcare professionals to refer to specialists (e.g., haematologists, specialists in coagulation) to diagnose and treat the condition.
    2.3. Knowledge and awareness of (updated) clinical guidelines and recommendations from learned societies for treating TTS (e.g., with anticoagulants), by learned society, by country, by dissemination method and date.
    2.4. Knowledge and awareness of the contraindication to use a second dose of adenovirus vaccine in patients who have experienced TTS after a 1st dose vaccination with Vaxzevria.

3. To determine the extent of change in **healthcare professionals**´ attitudes towards COVID-19 national vaccination campaigns and recommendations, by country, by age group, and by national vaccination strategy (i.e., through vaccination centre, general practitioner, specialist etc.).

4. To determine the extent of change in **citizens**' attitudes towards vaccination against SARS-CoV-2, by country, by age group, by gender, and if feasible, by type of regulatory action.

2. Work plan

The study consists of three work packages:

- **WP1** focuses on the national vaccination policies implemented in the EU member states included in this study.
- **WP2** regards the impact of the regulatory measures on healthcare professionals (HCPs), whereas
- **WP3** concerns the impact of the regulatory measures on the citizens/adults eligible to be vaccinated against COVID-19.

Setting

This is a multi-country study in six European countries: **Denmark** (DK), **Greece** (GR), **Latvia** (LV), **Netherlands** (NL), **Portugal** (PT) and **Slovenia** (SI)). The countries have a wide geographic spread, contrasting healthcare systems and cultures and a wide variation in vaccination policies following the EMA recommendations, namely:

- Discontinuation of administration of adenovirus vector vaccines in the national vaccination programme (Denmark).
- Changes to target group and prioritisation (Greece, Netherlands, Portugal).
- No alterations to previous established vaccination policies (Latvia).
- Temporary discontinuation of the Janssen vaccine in October 2021, followed by recommendation to use only mRNA vaccines (Slovenia).[1]

Selection of products

The study focuses on two adenovirus vector vaccines for active immunisation against COVID-19 (see Table 1). Both vaccines received a conditional marketing authorisation in the European Union in 2021.

Table 1 - Vaccines included in the study

Product name	Agency Product Number	INN Active ingredient	ATC-code
Vaxzevria (previously COVID-19 Vaccine AstraZeneca)	EMEA/H/C/005675	COVID-19 Vaccine (ChAdOx1-S [recombinant])	J07BX03
COVID-19 Vaccine Janssen	EMEA/H/C/005737	COVID-19 vaccine (Ad26.COV2-S [recombinant])	J07BX03

[1] As of November 30th, 2021, both Vaxzevria and the COVID-19 Vaccine Janssen are only available at patients' request (provided they are well-informed about the potential adverse effects) or in situations where SARS-CoV-2 mRNA vaccines are contraindicated.

Study design
Our study has a qualitative approach and is composed of three work packages involving a literature review, web-based questionnaires, and semi-structured interviews.

Work package 1 will compile an overview and timeline for national COVID-19 vaccination policies and any changes thereof prompted by the TTS risk communication. This includes changes to national vaccination policies, defining risk group(s), age group(s) prioritization, recommendations for second vaccine dose or for other SARS-CoV-2 vaccines.
The methodology in WP1 comprises a review of available (grey) literature and policy documents to identify the events and changes in vaccination policies in the countries participating in this study. National teams will gather information about vaccination policies (and changes) in their country. The EMA risk communication activities/events and the changes to national vaccination policies over time will be plotted per country and presented visually. The information about risk communication measures at national level will be gathered with support from the EMA, via national competent authorities.

In Work package 2 and Work package 3, we investigate the impact of the regulatory measures and communication and of the changes that occurred on national vaccination policies, on healthcare professionals (HCPs) and citizens eligible to be vaccinated against COVID-19.
The methodologic approach in WP2 and WP3 includes web-based questionnaires, to be hosted either nationally (DK, SI) or by Utrecht University (GR, LV, NL, PT), with subsequent quantitative and qualitative analysis. WP2 focusing on HCPs will also include the implementation of semi-structured telephone or online interviews.

2.1. WP 1: Document analysis to reconstruct timeline of events at national level

The country teams (see chapter 7) will conduct an online search for relevant documents on the national COVID-19 vaccination policy of their own country following instructions described in Appendix 1 and collecting information into the format provided in Appendix 2. They will analyse these documents to produce an overview and timeline for their national COVID-19 vaccination policies and any changes thereof prompted by the TTS risk communication. The implications and timelines of recommendations from the EMA and national advisory boards, will also be included in the overview.

The country teams involved in WP1 are the same as in remaining working packages and are detailed in chapter 7.

The coordination team will gather information about EMA activities, such as DHCPs, safety updates, and news items to establish a general EMA timeline on regulatory events with respect to Vaxzevria and the Janssen vaccine. The coordination team will also analyse the PRAC meeting highlights on the EMA website to collect details about the review of safety signals by PRAC. EMA provided relevant links to information on both vaccines, including assessment history on updates to the product information, safety updates, DHPCs, PRAC meeting highlights, news items published, and other recommendations related to TTS. Should there be questions regarding the EMA information, the coordination team will contact EMA for further clarification or support. The research team is aware that it will be important to use the correct terminology when describing the various regulatory documents and policy papers.

The country teams will gather information about events and vaccination policies in their own countries. In addition, where available/applicable, country teams are expected to collect any updated clinical guidelines and recommendations from learned societies for treating TTS.
A standard format to prepare the overview and timeline is included in Appendix 2, to map and assess developments in national COVID-19 vaccination policies and any changes ensuing from the

communication around the TTS risk. In addition to EMA data, information from national vaccination authorities, national medicines agencies and ECDC will be used, as well as that from national health authorities. EMA has also provided support in obtaining information by sending a Non-Urgent Information request to National competent authorities of the Member States involved in this study. This information will be used to corroborate data collected during the online search. If any specific questions relating to national vaccination policies exist and no public information is available to solve the issue, the coordination team may ask EMA to contact ECDC for support, as appropriate. EMA has provided the contractor with publicly available information on national vaccination campaigns, from the ECDC website.

2.2. WP2: Health care professionals' awareness and knowledge about the risk of TTS, their adherence to recommendations for SARS-CoV-2 adenovirus vector vaccines and their attitude changes towards national campaigns

Healthcare professional questionnaire

A web-based questionnaire will be used to gauge the HCPs' awareness and knowledge of the TTS risk and their perspective on the risk communication provided. A question whether the survey respondent is involved in the treatment of TTS will be added. This survey will also focus on eventual changes to attitudes following the 2021 regulatory recommendations on the risk of TTS after vaccination against COVID-19 with adenovirus vector vaccines.

This web-based questionnaire will be adapted to the various target groups, considering the healthcare professionals who are responsible and/or involved in the vaccination against COVID-19. When possible, we will also include healthcare professionals involved in the treatment of adverse events from COVID-19 vaccination. Given the variation in health systems across Europe, healthcare professionals involved in (mass) vaccination can be general practitioners, physicians working at Public Health Services, national or local health authorities, and when applicable, specialists or other HCPs. The sample is likely to vary per Member State. For instance, in some countries, pharmacists and/or veterinaries can vaccinate the public against COVID-19, whereas in other Member States they are not authorized to do so. An inventory has been conducted per country to identify and recruit the most relevant professionals using professional networks. As the study has a qualitative design, a proportional representation of different HCP categories in the response to the survey is not envisaged. Furthermore, the researchers consider that it is not feasible to obtain a proportional representation of the various HCP categories given the variability and complexity in the implementation of the immunization campaign across the different countries.

For the web-based questionnaire, relevant HCPs will be approached for participation in 5 countries (GR, LV, NL, PT, SI). Since the adenovirus COVID-19-vaccines were halted in Denmark, the health professionals survey will not take place in this country. Respondents will be recruited through professional associations and/or national health service directories in each country. We aim to have at least 500 healthcare professionals' responses in total, with 50-150 completed questionnaires per country, according to the country's population. In a country with a lower number of inhabitants, the community of physicians is smaller. We expect that in less-populated countries saturation will be more rapid as communication in a smaller community can be more homogeneous.

Member State (million inhabitants)	Minimum target of completed questionnaires by HCPs
Latvia (1.9)	50

Slovenia (2.1)	50
Portugal (10.3)	125
Greece (10.6)	125
Netherlands (17.3)	150

This descriptive study does not aim to provide a quantitative measurement. Our proposed methodology assumes that by completing 50 to 150 questionnaires per country saturation will be achieved. In qualitative study design, saturation implies that no new information is obtained when additional respondents are included[2]. The maximum variation (purposive) sampling is intended to reveal a spectrum of knowledge, awareness about and attitudes towards the TTS risk, thus we expect that data from 500 completed surveys will be sufficient to reach saturation and to display the variety in participating member states. Since we aim to characterize knowledge and behaviour in a specific group (HCPs involved in Covid-19 vaccination), we consider non-probability sampling (convenience sample) to be acceptable.

Web-based questionnaires will be developed using both open and closed questions. The survey will also allow respondents to write free text. This enables additional qualitative content analysis. Potential limitations and sources of bias are further discussed under item 5.

These questionnaires will be first developed in English, then jointly reviewed, then translated into Dutch and pilot tested only in the Netherlands due to the study's tight timeline. The content of the questionnaire will be developed in a manner to ensure content validity at EU level. We do not expect the questionnaire's content to be interpreted differently across different countries/languages, as it will be later adapted to reflect the country's situation. Furthermore, the validity of translations across the 6 countries will be ensured through back-to-back translations conducted by the panel of researchers involved at national level. Bearing these aspects in mind, we consider that a single pilot testing will suffice to uncover any weakness in design. Extending the pilot testing to other countries would imply an extension of the study timeline for other two months, as it would demand back-to-back translations in all participating countries. This would also require additional funding to cover extra resources.
After pilot testing, the questionnaires will subsequently be improved, translated back into English and then into the language(s) of the participating countries, as needed, according to protocol. (See Appendix 3).

To investigate the impact of the regulatory actions and communications thereof, as well as any subsequent policy changes, we will ask healthcare professionals to reflect on how these have affected their practice. Direct questions will be posed regarding their awareness of risks, attitude towards vaccination (e.g., discontinuation of a specific vaccine) before and after the policy alterations. Questions will be specifically formulated to include phrases such as 'before the changes' and 'after the changes,' and when available/applicable, we will include the specific change date, the national authority/body responsible for issuing the vaccination policy and a link to a description of the policy change.

The Healthcare professional (HCP) surveys will include questions to ascertain:

a. HCP's awareness and knowledge about the benefits and risks of the SARS-CoV-2 adenovirus vector vaccines.
b. HCP's awareness and knowledge about the risk of TTS.

[2] Saunders et al. Saturation in qualitative research: exploring its conceptualization and operationalization https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5993836/pdf/11135_2017_Article_574.pdf

c. HCP's knowledge of and adherence to SmPC recommendations for SARS-CoV-2 adenovirus vector vaccines and/or the recommendations on prevention of TTS included in vaccination instructions (as recommended by national vaccination authorities).
d. HCP's attitudes towards national vaccination campaigns and recommendations, and eventual changes thereof following the 2021 regulatory review.

Topics to include in the questionnaire will strive to cover:

(1) HCP's own working/vaccination duty context (vaccination centres, own medical practice, hospital).
(2) How they became aware of TTS (through media, professional society, direct healthcare communication, SmPC, instructions from authorities).
(3) Whether they received and were aware of the direct healthcare professional communications (DHPCs).
(4) Whether they have witnessed any TTS cases in their vaccination practice.
(5) Knowledge and awareness of the signs and symptoms of TTS and the need to refer to specialists (e.g., haematologists, specialists in coagulation) to diagnose and treat the condition; any instructions from vaccination authorities and/or national competent authorities for medicinal products and/or clinical practice guidelines when coming across TTS [3];
(6) Whether they have informed citizens about the TTS warning signs/symptoms and urged them to seek further health assistance should they occur.
(7) Knowledge and awareness of (updated) clinical guidelines and recommendations from learned societies for treating TTS (e.g., with anticoagulants) when available/applicable.
(8) Knowledge and awareness of the contraindications to use adenovirus vector vaccines in patients who have experienced TTS following vaccination with Vaxzevria.
(9) Whether and how the TTS risk communication has affected their attitudes towards the COVID-19 vaccination campaign and national vaccination programme in general.

Healthcare professional interviews

Deeper insight in the knowledge, attitude and perceptions of HCPs will be gained by conducting semi-guided (telephone or online) interviews.

The interviews with HCPs will provide additional in-depth information about how HCPs have perceived the timeline of events and the risk communication about the two adenovirus vector vaccines in their country. They will also be invited to reflect about their experiences, attitudes, and behaviour. Special attention will be paid to scope professionals' motivations and beliefs towards COVID-19 vaccination. This will provide details about personal views, which cannot be obtained through the survey. Since HCPs play a crucial role in reassuring and advising people about vaccinations, their perceptions about the risk communication will provide the PRAC greater insight into the impact of its recommendations in actual practice, as well as help explain any country differences.

The individual interviews will be conducted in six countries (DK, GR, LV, NL, PT, SI). This approach was chosen for practical reasons as it enables easier contract and scheduling, it conveys the possibility for professionals to talk more openly in their own language and to share information that would otherwise not be shared in group setting. Potential limitations of this methodological choice are further discussed under Item 5.

[3] Depending on country.

These interviews will be held with five to eight HCPs per country, professionals who were actively involved in vaccinating citizens against COVID-19 or treating any eventual adverse events arising from COVID-19 vaccination in the period between April and June 2021. When possible, we will also aim to interview a healthcare professional who has acted as decision-maker, thus responsible for adopting or adapting the EMA communication into national policies (through dedicated task forces, advisory boards, etc). We will identify the members of national task forces/expert advisory teams in each participating country and will invite the HCPs among them to participate. However, as the COVID-19 pandemic is still ongoing and these task forces/ expert advisory teams are still operational, their participation might be impaired.

A total of 30 – 48 participants from the interviews (5 to 8 participants per country) is considered sufficient to provide in-depth information and reach saturation for the total number of participants. A purposive sampling method to ensure heterogeneity of participants will be used. The researchers will strive to recruit HCPs across different specialities to diversify the responses obtained.

While we can expect HCP's availability to be limited due to the pandemic (as they are usually working overtime), we consider feasible to interview 5 to 8 HCPs per country. Conducting online interviews allows easier recruitment of HCPs as it facilitates efficient scheduling and is less time-consuming for interviewees and researchers. The intention of the interviews in general is to gain a better insight and more detail on the views and actions of HCPs regarding the Janssen and Vaxzervia vaccines and an opportunity for them to present their concerns, ideas, and questions. We expect that the total number of participants will be sufficient to provide rich in-depth information on how HCPs have perceived the events and the risk communication about the two adenovirus vector vaccines in their country and that differences between countries will be uncovered. When available, the preliminary results from the survey will be used to help develop the interview guide for the semi-structured interviews, i.e., the main version in English. The interview guide will be developed and reviewed by researchers. The interview guide will be pilot tested in NL. Once the English version of the final guide is agreed upon, national teams will adapt it to national settings and translate according to protocol (Appendix 2). The in-depth interviews will be held locally by national teams. Audio recordings will be transcribed verbatim.

Recruitment of professionals (per country)

We ran an inventory per country, to enable identification and recruitment of the most relevant professionals, including those specialities treating TTS in each country, when available. The information contained below provides information on eligibility of healthcare professionals per country.

Denmark (only applicable to interviews): general practitioners (recruitment via professional association and health authority newsletters), physicians and nurses from national and private vaccination centres (via contact points in these centres), emergency rooms (ER) at hospitals (contact points at ERs), and decision makers (via contact points at the Danish Health Authority).

Greece: In Greece, general practitioners, internists, and pulmonologists were mainly responsible for the vaccination at vaccination centres (either in public hospitals, primary healthcare centres or dedicated vaccination centres). Therefore, they were also those that directed patients to specialists when adverse events occurred (mainly haematologists). In addition, community pharmacists played a key role in providing guidance to citizens about their vaccination and potential risks, as vaccination scheduling was available at community pharmacies. Lastly, given that nurses were involved in administering the vaccine, but had no official consultation responsibilities, targeting this specific group of professionals in our survey is still open for discussion. Recruitment methods will include contact

with healthcare professional groups, e-mail lists for healthcare professionals, direct contact with heads of departments in hospitals or primary healthcare centres; healthcare professional groups on social media (Facebook, LinkedIn) and snowballing through already recruited healthcare professionals.

Latvia: General practitioners working in outpatient healthcare facilities or clinics with a contract with the Latvian national health service (NHS). We are planning to recruit GPs based on the publicly available NHS list of specialists/clinics providing vaccination. We will aim to include decision makers in semi structured interviews. TTS is treated mainly by GPs and haematologists. There are approximately 20 haematologists in Latvia, it is unlikely we will be able to recruit a meaningful number of responders.

Netherlands: general practitioners, haematologists and pharmacists will be recruited through existing networks and professional organizations via newsletters; physicians and nurses working at regional and municipal public health services involved in vaccination programmes will be recruited through direct contact from the National Institute for Public Health and the Environment (RIVM). For the interviews we also plan to invite experts from the national pharmacovigilance centre.

Portugal: In Portugal, COVID-19 vaccines were administered by nurses, and the diagnosis and treatment of TTS were performed by physicians, mostly by clinical haematologists but also by other categories such as internal medicine, GP, vascular surgery, neurology, among others. In addition, community pharmacists were frequently approached by the population to clarify the signs and symptoms associated with TTS, and guidance was provided on the risks associated with vaccination. We would therefore be interested in also including this professional group. The recruitment strategy for the healthcare professionals' online questionnaire will include professional networks, collaboration with professional associations (Pharmacists, Physicians and Nurses) and social media. For telephone interviews, we intend to recruit Healthcare Professionals from different settings (physicians from distinct categories, pharmacists, and nurses) using professional networks or associations.

Slovenia: In Slovenia, general practitioners and nurses were involved in the vaccination. Treatment of TTS was primarily performed by clinical haematologists, but also internal medicine specialists and general practitioners, among others. As information regarding the effectiveness and safety of vaccines, including TTS, was often sought, and provided in local pharmacies, we also aim to include community pharmacists in our surveys. For the interviews we also plan to invite decision makers and public health experts, involved in the national COVID-19 vaccination strategy.

2.3. WP3: Mapping citizen awareness and measuring citizen knowledge about TTS

Citizen questionnaire study

A web-based questionnaire will be conducted in a sample of citizens to measure their attitudes towards vaccination against SARS-CoV-2 and more specifically, their attitudes as to vaccination with adenovirus vector vaccines and their risk perception about TTS. The data from these national citizen questionnaires will enable an analysis by age group, gender and COVID-19 risk group. Questions will be formulated to obtain as much information as possible about the influence of the various regulatory actions of adenovirus vector vaccines and their effects on citizens' attitudes. Each of the six participating countries (DK, GR, LV, NL, PT, SI) selected the most suitable strategy to obtain a sample representative of their country's adult population. The various recruitment possibilities were discussed during joint meetings before deciding at national level. The minimum target of citizens to recruit will consider the country's population, but we aim to include at least 100-200 subjects per country, with a minimum of 900 citizens in total. For this descriptive study, we expect that this

respondent population will be sufficiently large to display the variety in attitudes towards COVID-19 vaccination.

Member State (x million inhabitants)	Minimum Target of completed citizen questionnaires
Latvia (1.9)	100
Slovenia (2.1)	100
Denmark (5.9)	150
Portugal (10.3)	175
Greece (10.6)	175
Netherlands (17.3)	200

Again, direct questions will be posed regarding citizens' awareness of risks, their risk perceptions both about COVID-19 infection and about risks from COVID-19 adenovirus vector vaccines, their attitude towards vaccination (e.g., discontinuation of a specific vaccine) before and after the policy alterations. Questions will be specifically formulated to include phrases such as 'before the changes' and 'after the changes,' and when applicable, we will include a specific change date and a link to a description of the policy change.

Topics to include in the questionnaire will strive to cover:

(1) Respondent characteristics: age, gender, belonging to a risk group for COVID-19 and/or a professional group with vaccination priority according to the national vaccination policy.
(2) Date at which they were invited for vaccination.
(3) Present status of vaccination against COVID-19 and period of first and second vaccination.
(4) Vaccine(s) received;[4]
(5) Awareness and perceptions about the benefits and risks of the SARS-CoV-2 adenovirus vector vaccines.
(6) Awareness and perceptions about the risk for TTS from adenovirus vector vaccines.
(7) Source of information about the risk for TTS.
(8) Awareness about changes in COVID-19 vaccination policy and their impact on own perceptions and attitudes regarding vaccination against COVID-19.
(9) Changes to own attitudes towards vaccination against COVID-19 and use of COVID-19 vaccines: no vaccination against COVID-19, postponement of vaccination, decision to change vaccine.
(10) Changes to own attitudes towards potential vaccination of their young adult-teenager children against COVID-19.
(11) Changes to own attitudes towards vaccination programmes in general.
    i. positive, hesitant, negative both before and after the initial COVID-19 vaccination campaign.
    ii. positive, hesitant, negative both before and after the COVID-19 vaccination booster campaign
(12) Changes to own attitudes towards general children vaccination programmes.
(13) Willingness to receive future (booster) vaccination(s) against COVID-19.

These questionnaires will be first developed in English, then jointly reviewed, then translated into Dutch and pilot tested in the Netherlands. They will subsequently be improved, translated back into

[4] Our recruitment does not restrict respondents to citizens who have received adenovirus vaccines. We are also interested in finding out whether citizens' choice of vaccine/or their decision not to take vaccine has been affected by the risk communication.

English and then into the language(s) of the participating countries, as needed, according to protocol (Appendix 2). Due to the tight study timeline pilot testing in more than one country is not feasible. However, the pilot testing in the Netherlands will provide information on essential ambiguities in the questions and will improve survey quality. The translation of the survey into the six different national languages will be conducted according to the translation protocol (Appendix 2). The protocol foresees an independent review of each translated survey by a native speaker not involved in the study team. In doing so, we aim to identify culture- and language-specific issues to enable adjustment when needed.

Each of the six participating countries (DK, GR, LV, NL, PT, SI) has selected the most suitable strategy to obtain a sample of their country's adult population, as described below. We will aim to recruit diverse responders to include different sociodemographic subgroups of adult population.

It should be noted that given this is a qualitative study, the goal is that of obtaining a breadth of responses which reflect the diversity in attitudes and behaviours that are to be found in each country. Given the varying sampling methodologies, overall representativeness cannot be guaranteed. Nevertheless, we will strive to have all sociodemographic groups represented in each country through methods described below.

Denmark: Citizens will be recruited through social media. This effort will be targeted so that those who first receive the links belong to different ages and educational backgrounds then recruitment will occur through snowballing (asking recipients to forward the link).

Greece: In Greece, no service nor specific platform is available to collect a representative sample and there is limited time available for recruitment. Therefore, we will firstly recruit citizens through social media platforms (Facebook, blog forums). This approach is common in qualitative studies with restricted timelines, as it yields a good response and targets varied age groups and socioeconomic /educational backgrounds. Secondly, cards/leaflets with the QR code or link to the online questionnaire will be distributed in venues visited by citizens such as municipalities, community pharmacies, primary health care settings, etc. This will allow outreach to citizens who might not be familiar with social media platforms. As a back-up strategy the Greek research team is planning to collect questionnaires using portable electronic devices (laptops/tablets) by approaching citizens at public venues (subject to ongoing COVID-19 mitigation measures). This last approach will facilitate surveying citizens less familiar with technology (elderly groups, people with IT difficulties, etc) and allow them to complete the questionnaires.
Latvia: We plan to use snowball sampling via social media, online groups, and mailing lists to obtain a sample that represents diverse sociodemographic subgroups of the general population. Since this study does not aim to provide a quantitative measurement, we consider that snowball sampling is appropriate to capture wide range of views from different socioeconomic groups. As a back-up plan, we will recruit responders via community pharmacies and primary care practices.

Netherlands: We plan to use a citizen research panel, outsourcing through an independent research company specializing in public opinion research, to obtain a representative sample. The independent research company operates an extensive citizen research panel. The characteristics of panel members are known to the company which then selects a sample representative of the Dutch population. The company is a designated supplier selected by RIVM and applies validated strategies to reach the target response.

Portugal: Recruitment is likely to occur through social media, namely through publication of the questionnaire on social networks (Facebook, LinkedIn), targeting websites, sending the questionnaire to contact lists, among others. Although snowball sampling via social media can imply some bias, we are unable to use online panels. We do not foresee selection bias when using contact lists as we will

not use prespecified lists related to vaccination, but the mailing lists from our home institutions (two Portuguese universities). These contact lists include individuals from different age groups, socioeconomic strata, and education levels (academia, administrative and technical staff, study assistants, housekeeping services, etc.).

Slovenia: We plan to use "online panels," from one of the agencies providing services in market/social/public opinion research. Such panels are highly responsive. They are also weighted according to the population characteristics (e.g., age, gender). As a back-up strategy we have planned to use an alternative agency to provide an "online panel" or to recruit citizens via social media platforms (Facebook, blog forums).

2.4. Data Analysis

WP 1 - Each National Team (NT) will provide the overview and timeline of COVID-19 vaccination policies to the Study Coordinator (SC) for compilation according to a standardized and agreed format. These will consist of data collection and grey literature review. These overviews will be scheduled for the start of the project to provide input to the drafting of the surveys and the interview/ guides. The EMA risk communication activities/events and the changes to national vaccination policies over time will be plotted per country and presented visually.

The surveys in **WP2** and **WP3** will generate descriptive statistics, univariate and bivariate analyses will be conducted according to stratifying variables, where applicable. Given the variation in vaccination policies and the need to tailor questionnaires to participating countries, survey data will be analysed at national level. For the qualitative data, the analysis involves a deductive content analysis based on a close line-by-line reading of the responses and developing a conceptual coding scheme based on the major themes in the interview guides. Transcripts will be coded individually by two researchers in each country in their native languages. Coders from all countries will meet prior to the analysis to predefine categories and codes to be used. They meet again to evaluate the categories identified and to write up the results using illustrative quotes.

Processing of personal data will comply with the EU data protection legislation and in particular Regulation EU 679/2016 on General Data Protection. Citizens and healthcare professionals will participate anonymously in the questionnaires.

All data will be either collected anonymously or anonymized by the national teams. This means that no data that can identify individual citizens or HCPs is to be collected (e.g., name, address, social security number).

For HCPs who accept to be contacted for the in-depth interviews, their identification will be kept encrypted to comply with the General Data Protection Regulation.

Only fully anonymized data will be shared with the coordinating team. National teams will also be responsible for ensuring (obtaining, compiling, and archiving) ethical approval and participants' informed consent. The coordinating team will provide a template for an informed consent form in English for both groups of respondents, healthcare professionals and citizens, respectively.

3. Organisation of work

3.1 The teams/people involved

The Coordinating Team (CT) is composed by:

- Dr Teresa Leonardo Alves and Dr. Ingrid Hegger, Researchers at the Centre for Health Protection, National Institute for Public Health and the Environment, The Netherlands.

- Prof. Anna Birna Almarsdóttir, Research leader at the Social and Clinical Pharmacy research group, Department of Pharmacy, Faculty of Health and Medical Sciences, University of Copenhagen, Denmark.

- Dr E.R. (Rob) Heerdink , Associate professor of Clinical Pharmacoepidemiology at the Division of Pharmacoepidemiology and Clinical Pharmacology of the Department of Pharmaceutical Sciences, Utrecht University, The Netherlands.

The National Teams (NTs) are represented in the Steering Committee by:

- Denmark: Prof. Anna Birna Almarsdóttir, Research leader, Dr. Ramune Jacobsen, Assistant Professor, Department of Pharmacy, University of Copenhagen
- Greece: Dr Christos Kontogiorgis, Assistant Professor, Democritus University of Thrace, Department of Medicine, Laboratory of Hygiene and Environmental Protection.
- Latvia: Dr Elita Poplavska, Assistant Professor, The Institute of Public Health of Riga Stradins University.
- Portugal: Dr Inês Ribeiro Vaz, Coordinator, Unidade de Farmacovigilância do Porto, Faculdade de Medicina da Universidade do Porto.
- The Netherlands: Dr Ingrid Hegger, Expert Researcher, the Centre for Health Protection, National Institute for Public Health, and the Environment.
- Slovenia: Prof. Mitja Kos, Head of Department of Social Pharmacy, and Assist. Dr Nanča Čebron Lipovec, both: University of Ljubljana, Faculty of pharmacy, Ljubljana.

The Study Coordinator (C) is:

- Dr Teresa Leonardo Alves, Researcher at the Centre for Health Protection, National Institute for Public Health and the Environment, The Netherlands.

The Steering Committee is composed by:

- one representative per country and one alternate per country (back-up).
- chair / vice-chair: SC and alternate.

The coordinator of the consortium is:

- Prof. Olaf Klungel, Division of Pharmacoepidemiology and Clinical Pharmacology, Utrecht University, The Netherlands.

3.2 Timelines and tasks

The study started in **M1** with an online kick-off meeting organised by the Study Coordinator (SC), during which all those involved in the project became familiar with their counterparts in other countries and the study coordinator. The Coordinating Team (CT) is responsible for hosting and preparing the content discussions, which will cover communication aspects, data management, and compliance with timelines and feedback procedures. An email-distribution list has been established

to share information among all those involved, and telephone and online meetings are scheduled on a regular basis to oversee project implementation and progress.

During M1, the development of the study plan has been initiated by the Coordinating Team, but National Teams (NT) were invited to review and provide input. A similar procedure will be implemented for the study protocol in **M2**.

In M1, a standard format to prepare the overview and timeline has been drafted by the SC and agreed upon by the CT and NTs. During M2, the NTs will be responsible for providing the overview and timelines of the COVID-19 policies in their own country. These overviews will provide important background information to the surveys and the interview guide. These national overviews will be compiled later in M3 into an overall overview by the Study Coordinator and will be subsequently reviewed by the Coordinating Team and the National Teams.

In M2, the Dutch national team based in Bilthoven (RIVM) is responsible for developing the first draft of the healthcare and patient questionnaires in English. These will be subsequently reviewed by the Coordinating Team and the National Teams.

In M4, The Dutch team will translate them into Dutch and pilot test them in the Netherlands in a small sample of healthcare professionals and citizens. The questionnaires will subsequently be improved, translated back into English and then into the language(s) of the participating countries, as needed, according to protocol.

Between M4 and M5, National Teams will include seeking Ethical Approval providing the translated final questionnaires.

All National Teams are also invited to start recruiting respondents **from M5 onwards**, as this is the most limiting factor for a successful implementation. Recruitment of participants and survey implementation are likely to overlap between M5 and M6. Throughout the questionnaire implementation and data analysis, the Coordinating Team will schedule online meetings to receive feedback on project progress.

Between M5 and M6, National Teams will recruit HCPs for interviews and conduct the interviews.

Between M6 and M7, each National Teams is expected to analyse their local data. The coordinating team will compile those and compare results across countries, when applicable.
All the analyses are expected to have been delivered to the Coordinating Team.

Between M6 and M9 the Coordinating team will take the lead on the reporting, drafting both the preliminary report and the preliminary manuscript. Both documents will also be reviewed by the national teams, and if deemed necessary, by the European Medicines Agency responsible staff.

The timeline described below provides an overview of the study chronology together with main tasks, including responsible teams, identifying also the main milestones (indicating project progress) and deliverables. It can be subject to adjustments, as necessary.

Timing:
M1 to- M10 = 10 months

Milestones:

M1: Milestone 1: National overviews of COVID-19 vaccination policy available
M2: Milestone 2: Draft questionnaires in pilot phase
M3: Milestone 3: Questionnaires ready to be implemented
M4: Milestone 4: Recruitment of Respondents completed
M7: Milestone 5: Coordinating team receives all the data analysis from NTs
M8: Milestone 6: Draft Report has been written and agreed upon by NTs and CT
M9: Milestone 7: Draft Manuscript has been written and agreed upon by NTs and CT

Deliverables:
D1: Deliverable 1 Preliminary Study Plan
D2: Deliverable 2 Study Protocol
D3: Deliverable 3 Study Report
D4: Deliverable 4 Manuscript

People involved:
CT: Coordination team
NT: National teams
NL: Netherlands team

TIMELINE	M1	M2	M3	M4	M5	M6	M7	M8	M9	M10
Project inception										
Organization kick-off meeting	CT									
Kick-off meeting Installation Steering Committee	CT NT									
Development of preliminary study plan	CT NT	CT NT								
Study plan delivery		**D1**								
Development of standard format overview COVID-19 vaccination policy	CT									
Development of instructions for recruitment forms and of harmonized consent forms	CT									
Developing overview and timeline COVID-19 vaccination policy	NT	NT	NT	NT						
Development of questionnaire health care professionals	NL	NL CT	NL CT							
Development of questionnaire citizens	NL	NL CT	NL CT							
Writing and reviewing protocol		CT NT	CT NT							
Protocol delivery		CT	CT **D2**							
Registration of study and protocol in EU PAS Register	CT	CT	CT							
Monitoring progress	CT	CT	CT	CT	CT	CT	CT	CT	CT	
Data collection and analysis										
Pilot testing of questionnaire healthcare professionals			NL	NL M1						
Pilot testing of questionnaire citizens			NL	NL M1						
Tailoring questionnaires to national setting and translating				NT	NT					
Seeking Local Ethical Committee Approval					NT					
Hosting web-based questionnaires					CT					
Recruitment of respondents - healthcare professionals					NT	NT				

TIMELINE	M1	M2	M3	M4	M5	M6	M7	M8	M9	M10
Recruitment of respondents - citizens					NT	NT	NT			
Implementation questionnaire healthcare professionals					NT	NT	NT			
Implementation questionnaire citizens					NT	NT	NT			
Data analysis questionnaires and delivery					NT	NT	NT M3			
Compiling overviews and timelines COVID-19 vaccination policies				CT	CT					
Development of interview guide			CT				CT			
Recruitment of HCPs for interviews in 6 countries					NT	NT	NT			
Interviews HCPs in 6 countries					NT	NT	NT			
Data analysis interview and delivery							NT			
Monitoring progress	CT	CT	CT	CT	CT	CT	CT	CT	CT	
Reporting										
Drafting preliminary report						CT	CT	CT M4		
Review of draft report								CT NT		
Delivery of final report									CT **D3**	
Drafting manuscript							CT	CT	CT M5	
Manuscript review									CT NT	
Manuscript delivery										CT **D4**

3.3 Project management & communication: The coordinating team has installed a steering committee in which all countries involved are represented by 1 person and an alternate person (back-up). This committee is chaired by the coordinator of the study (RIVM) who is responsible for organization of meetings (Face-to-Face, tele- and/or web-conferencing) including detailing of agendas, distributing of meeting minutes. An alternate coordinator (back-up) has also been nominated among the committee to ensure continuity.

Liaison with the European Medicines Agency is ensured by the coordinator of the consortium, Prof. Olaf Klungel, since he is the principal contact with regards to the Framework service contract. Meetings between the Agency to discuss the study will be organized at critical moments during the contract (start of contract, final study protocol, results of analysis, study report). These will be attended by the members of the Coordinating team and Committee, as deemed necessary. More frequent meetings can be organized at the request of the Agency or the consortium.

4. Quality Control

Tailored quality control: The coordinating team will rely on a peer review model of consultation to inform and direct the study deliverables using the timeline above to monitor and benchmark progress by which outcomes are assessed. To establish a quality control system specific to this study, we have identified key milestones which will attest to the efficient roll-out and continuity of the service.

These are, respectively:

- M1: Milestone 1: Citizens' and HCPs' Questionnaires available
- M2: Milestone 2: Recruitment of Respondents completed
- M3: Milestone 3: Coordinating team receives all the results from national analyses from NTs
- M4: Milestone 4: Draft Report
- M5: Milestone 5: Draft Manuscript

In addition, we also provide below a list of verifiable indicators along the timeline:

Specific Task	Standard Verifiable Indicators
Kick-off meeting	Agenda Meeting Minutes Action Points Agreed Timeline
Development of questionnaire	Draft questionnaire
Pilot testing of questionnaire	Pilot questionnaire and final version of questionnaire
Recruitment of respondents	Number of healthcare professionals and citizens recruited per country
Implementation questionnaire	Response rates (monthly)
Interviews in key countries	Interview/ guides
Drafting preliminary report	Preliminary Report
Review of draft report	Responses received
Drafting manuscript	First draft manuscript
Manuscript review	Responses received

Overarching quality control: Several quality assurance measures are in place that will be maintained in the proposed consortium. We will take into consideration existing guidelines for qualitative research (such as QOREC) and apply them as appropriate. Additionally, we will share approaches to

data collection and analysis. Deliverables are peer-reviewed by an advisor (at least one member of the consortium that is not leading nor actively participating in the study). A declaration of competing interests will be required from all those acting as principal investigators or co-investigators. These will be further presented to the Steering Committee who will then assess and act upon any potential conflict of interest. In addition, we aim to comply with ENCePP standards. We have registered our study on the European Union electronic Register of Post-Authorisation Studies (EU PAS 44970) and aim to apply for the ENCePP Study Seal.

Quality management system for the Coordinator of the consortium (Utrecht University): The Division of Pharmacoepidemiology & Clinical Pharmacology works according to a quality management system based on ISO 9001 principles. The quality management system is system and process oriented and based on continuous improvement. All primary and secondary processes within the division are included in the quality system, from creating research proposals, through managing PhD projects to data management, reporting and archival. The system is based upon standard operating procedures implemented throughout the division with regular internal audits as well as external audits that lead to certification. The quality management system is based on national and international external quality requirements where available and pertinent, as well national, and international guidelines and legislation concerning data-handling and privacy issues.

Research Quality Assessment (Utrecht University): In 2017 (evaluation period 2010-2015), the research quality of the Utrecht Institute for Pharmaceutical Sciences (UIPS) which includes the division of Pharmacoepidemiology & Clinical Pharmacology was assessed by an independent international peer review committee according to the Standard Evaluation Protocol 2015-2021 (SEP) for Research Assessment in the Netherlands. The overall conclusion of the committee was that the division was one of the top ten if not the top five worldwide and that excellent scientific work was being done, grounded in real-world problems and with a notable impact on the regulatory world, particularly in Europe. The scores received were all excellent for the Quality, Relevance to Society and Viability criteria. This report is available upon request.

5. Strategies to prevent or counter any events that could hamper or delay the research

Foreseen external delays, methodological or technical problems and their proposed counter measures:

- **Specific requirements for ethical approval for research and data protection** regulations are to be addressed at protocol stage, considering national and European settings.
- To avoid **delays in ethical approval**, the questionnaires will be submitted in English, when possible.
- Given the tight study timeline, **pilot testing in more than one country is not feasible**. The translation of the survey into the six different national languages will be conducted according to the translation protocol (Appendix 2). The protocol foresees an independent review of each translated survey by a native speaker not involved in the study team. In this manner, we aim to identify culture- and language-specific issues to enable adjustment as needed.
- To avoid **delays in the questionnaire implementation**, recruitment will be initiated as early as possible.
- **Recruitment of specialists** involved in the provision of guidance or treatment of adverse events arising from COVID-19 vaccination might prove difficult to recruit in less populated countries, where the number of specialists is reduced. The solution will then include an oversampling of other healthcare professionals meeting our inclusion criteria.

- To avoid **delays in data analysis**, specific instructions will be delivered to the country researchers. In exceptional circumstances, the coordination team can resort to directly analyse the data which is stored in the centralized survey database.

Study limitations	**Definition**	**Applicable to**	**Mitigation strategy**
Recall bias	Recall bias occurs when there are systematic differences in the way subjects remember or report exposures or outcomes.	Web-based questionnaires and interviews. Although the current study will use a semi-qualitative descriptive design, recall bias might still occur. Any baseline attitudes of healthcare professionals and patients towards Covid-19 vaccination might now be recalled differently due to the later occurrence of thrombosis events after Vaxzevria or COVID-19 Janssen vaccination and due to their vast media coverage. Communications, safety updates and product information changes by the EMA conducted during 2022[5] might also impact on how participants respond to the questionnaires and interviews.	Recall bias can be an issue, when there is no baseline measurement and when all parameters are to be ascertained retrospectively. However, we will consider this limitation when interpreting our results by considering the direction of the bias on our findings.
Information bias - Hawthorne effect	There is a change in behaviour of research participants in an experimental or observational study, due to the interest, attention, and care that they receive from the researcher	Interviews. Participants' opinion about our outcome of interest might be influenced by the mere fact of being questioned about it by a researcher.	This is a general obstacle in every qualitative study using interviews, but we do not expect a significant effect from this bias on our results if we coordinate efforts to train interviewers.
Selection bias – Country differences	National differences in the healthcare systems of the countries included in this study might also imply differences in information dissemination to healthcare professionals and the public at large.	Web-based questionnaires and interviews.	Consider this limitation when interpreting our results by considering how the variation in health systems might affect our findings.

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Study limitations	Definition	Applicable to	Mitigation strategy
Non-responder bias	It implies that non-responders to the survey can have other characteristics than the responders.	Web-based questionnaires and interviews. For instance, it could prove challenging to include older people into the web-based survey since many elderlies are not familiar with computer use. Furthermore, it might be difficult to include respondents from vulnerable population groups which are also more vulnerable to COVID-19, such as people suffering from mental disorders, or people with low health literacy.	At RIVM in the Netherlands, a special research unit studied the Dutch population's behaviour during the COVID-19 pandemic. This offers us useful information to assess biases in our study results. We will also investigate data available from other national surveys focusing on population behaviour in other Member States, when available. As TTS is a side effect occurring in younger groups, we do not expect that a lower participation of elder population will impact on our results.
Response bias – Acquiescence or agreement bias	Respondents tend to select a positive response option or indicate a positive connotation disproportionately more frequently.	Web-based questionnaires and interviews.	Introducing carefully crafted, open-ended questions and carefully working closed-ended questions and response categories to increase the probability of nuanced and varied responses.
Response bias - Extreme responders	It drives respondents to only select the most extreme options or answers available.	Web-based questionnaires and interviews. We may obtain an overrepresentation of persons who are very engaged or opinionated one way or another about these vaccines.	This may be culturally driven; the team will look at whether this is a phenomenon varying by countries.

Study limitations	Definition	Applicable to	Mitigation strategy
Response bias - Question order	A respondent may react differently to questions based on the order in which questions appear in a survey or interview.	Web-based questionnaires and interviews.	The research team will be vigilant about not skewing views we order the questions.
Response bias - Social desirability	Tendency of survey respondents to answer questions in a manner that will be viewed favourably by others.	Web-based questionnaires and interviews	The wording of question needs to be extremely balanced, non-judgemental so that vaccine hesitant persons can respond.

6. Plan of operations

Project Stage (% overall study)	Coordinating Team % of specific task	National Teams % of specific task	Coordinating Team % of overall study	National Teams % of overall study
Project Inception (30)	80	20	24	6
Data Collection and Analysis (55)	20	80	11	44
Reporting (15)	80	20	12	3
TOTAL:100%			47	53

7. Further information about the investigators

This section provides an overview of all the teams involved, both in the coordination and per country, including their background and expertise, as well as contact details.

Country: Denmark

Description of the institution (including location): Social and Clinical Pharmacy (SCP) is a research group under the Department of Pharmacy, Faculty of Health and Medical Sciences, at the University of Copenhagen. SCP's research is within three broad topic areas of Medicines Use, Clinical Pharmacy, and Pharmaceutical Policy. Research within each focus area can be situated on one or more of the levels of the user, organization, and society.

Description of the research team/researcher(s) involved as to their background, competences, and interests (Country Team DK):

- Anna Birna Almarsdóttir is Professor in Social and Clinical Pharmacy. She has more than 25 years of experience with social and clinical pharmacy research, which have included areas such as health services research, pharmacoepidemiology, and drug utilization research. Her focus is currently on developing clinical pharmacy services (in the primary, secondary and tertiary health care sectors), and pharmaceutical policy analysis using both qualitative and quantitative research methods. Her methods interests are questionnaire construction, scale development, and triangulation of qualitative and quantitative research methods. She graduated as PharmD from the University of Iceland in 1988 and received a PhD degree in Health Policy Analysis in 1994 from the University of North Carolina at Chapel Hill, USA. Her work experience includes Assistant and Associate Professorships in Clinical Pharmacy, at the Royal Danish School of Pharmacy and the University of Iceland, and Professorships at the University of Iceland and the University of Southern Denmark. In addition, she held a position as Senior Pharmacoepidemiologist at DeCode Genetics Inc and consulted with the pharmaceutical industry in Iceland.
- Ramune Jacobsen is an Assistant Professor in Clinical pharmacy; she has more than 15 years of experience with social pharmacy and public health research, including implementation and evaluation research in health services for chronic disease management, epidemiological research in disease prevention, and survey-based research for health promotion. She graduated as a Master in Medical Biology in Moscow (Russia) in 1994, and as a Master of Public Health in Kuopio (Finland) in 2003 and earned her PhD in Social Pharmacy in 2010 in Copenhagen (Denmark).
- Caroline Buhl.

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Country: Greece

Description of the institution (including location): Our Laboratory of Hygiene and Environmental Protection belongs to the Faculty of Medicine, School of Health Sciences, Democritus University of Thrace, Alexandroupolis, Greece. It presents an extraordinarily strong background on epidemiological studies and preliminary experience on pharmacoepidemiologic analysis and data analysis.

Description of the research team/researcher(s) involved as to their background, competences, and interests (Country Team GR):

- Christos Kontogiorgis, Assistant Professor has experience in pharmacoepidemiologic studies.
- Theodoros Constantinides, Professor is an expert in epidemiological studies and statistical analysis.
- Evangelia Nena, Associate Professor, expert on epidemiological studies and statistical analysis.
- Elena Deligianni, Pharmacologist, MSc, PhD student has expertise in pharmacoepidemiologic analysis and drug utilization studies.
- Chara Oikonomou, PharmD with expertise in pharmacoepidemiologic analysis and drug utilization studies.
- Foteini Dermiki-Gkana, PharmD, presents expertise in epidemiological analysis and drug utilization studies.

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Country: Latvia

Description of the institution (including location): The Institute of Public Health of Riga Stradins University is in Riga, the capital of Latvia. The objective of the RSU Institute of Public Health is to carry out research, undertake academic training and promote the acquisition and improvement of scientific qualifications in public health and healthcare organization. The institute has research expertise in areas such as sexual and reproductive health, HIV, diabetes, nutrition, pharmaceutical policy, health systems, economics, and many others.

Description of the research team/researcher(s) involved as to their background, competences, and interests (Country Team LV):

- Elita Poplavska, PhD is an assistant professor at the Faculty of Pharmacy and senior researcher at the Institute of Public Health. She holds a PharmD from Riga Stradins University and a PhD in Social and Administrative Pharmacy, University of Minnesota. Her research activities are related to pharmaceutical policy, medicines use research and pharmaceutical promotion involving qualitative and quantitative research methods.
- Mirdza Kursite, MD, MS is a lecturer at the Faculty of Public Health and Social Welfare. She holds an MD and Master's degree of Health Sciences in Health care from Riga Stradins University. Her research activities are related to patient - physician communication, adherence to therapy and health beliefs involving qualitative and quantitative research methods.

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Country: Portugal

Description of the institution (including location): Porto Pharmacovigilance Centre (PPC) is a Portuguese regional pharmacovigilance centre, part of the National Pharmacovigilance Centre which coordinated by Infarmed (National Authority of Medicines and Health Products, I.P.). PPC is based on the Department of Community Medicine, Information and Health Decision Sciences of the Faculty of Medicine of the University of Porto since its creation in 2000. The PPC covers a region with 1.8 million inhabitants and 24000 healthcare professionals and works closely with healthcare institutions, namely hospitals, primary health care units and community pharmacies.

Description of the research team/researcher(s) involved as to their background, competences and interests (Country Team PT):

- Inês Ribeiro Vaz has a Doctorate degree in Clinical Research and Health Services, awarded by the Faculty of Medicine, University of Porto in 2016 with the thesis: "Using Information Systems in Pharmacovigilance. She has a Master on Public Health awarded by the Faculty of Medicine, University of Porto in 2009. Has a degree in Pharmaceutical Sciences awarded by the Faculty of Pharmacy, University of Porto in 1999. Performs duties as technical and scientific coordination of the Porto Pharmacovigilance Centre since 2003 and, over the last 15 years, has published several papers, both as author and as co-author, in pharmacoepidemiology, pharmacovigilance and drug safety.
- Ana Marta Silva is also a pharmacist working at Porto Pharmacovigilance Centre since 2013. During this year, she has been working extensively on the pharmacovigilance of vaccines against COVID-19. She is a PhD student with an ongoing thesis about the impact of COVID-19 in pregnant women.
- Paula Barão has a Master in Pharmaceutical Care awarded by the Faculty of Pharmacy, University of Lisbon in 2013 and a degree in Pharmaceutical Sciences awarded by the Faculty of Pharmacy, University of Lisbon in 1995. She works as a pharmacovigilance expert at the Lisboa, Setúbal and Santarém Pharmacovigilance Centre since 2011 and is a PhD Student with an ongoing thesis about risk minimization measures on pregnancy.

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Country: Slovenia

Description of institution (including location): Faculty of Pharmacy (FFA), University of Ljubljana (UL) is the only university organization in the Republic of Slovenia for the study of pharmacy and laboratory biomedicine. The Faculty of Pharmacy follows the concept of scientific pharmacy and clinical biochemistry and considers research and study as two inseparable parts. By European standards FFA is a medium-sized faculty. Yearly it admits 150 students of Uniform master's study program Pharmacy, 40 students at University study program Laboratory Biomedicine, 40 students at University study program Cosmetology, 40 students of Master's study program Laboratory Biomedicine, 25 students of Master's study program Industrial Pharmacy, and about 30 students of 3rd cycle of Bologna study program Biomedicine. Established in 1997 the Chair of social pharmacy focuses on the development of academic and experimental grounds for education and research in the broader area of social pharmacy. The area of interest are the influences of drugs as material, biomedical, ethical, and proprietary category on the modern individual and society. Research includes pharmacoepidemiology, pharmacoeconomic and outcomes research. The Chair is devoted to the study of properties and development of information technology in acquisition and transfer of knowledge about medicines. It studies the role of pharmaceutical profession in the modern societies, and the methods of communications between pharmacists and other health professionals, and with lay public. Central concepts of interest are also patient counselling and pharmaceutical care.

Description of the research team/researcher(s) involved as to their background, competences, and interests

Established in 1997 the Department of social pharmacy focuses on the development of academic and experimental grounds for education and research in the broader area of social pharmacy. The area of interest are the influences of drugs as material, biomedical, ethical, and proprietary category on the modern individual and society. Research includes pharmacoepidemiology, pharmacoeconomic and outcomes research. The Department is devoted to the study of properties and development of information technology in acquisition and transfer of knowledge about medicines. It studies the role of pharmaceutical profession in the modern societies, and the methods of communications between pharmacists and other health professionals, and with lay public. Central concepts of interest are also patient counselling and pharmaceutical care.

Description of the research team/researcher(s) involved as to their background, competences, and interests (Country team SI):

- Prof. Mitja Kos, M Pharm: Mitja Kos is the Head of the Department of Social Pharmacy and a professor for social pharmacy at the University of Ljubljana, Faculty of Pharmacy, Slovenia. He graduated as a pharmacist in 1999 and defended his doctoral thesis on the topic of off label prescribing in 2005. He has developed expertise in several different fields including pharmacoeconomic and outcomes research, pharmacoepidemiology, medicine pricing and regulation and pharmaceutical care practice. The focus of his scientific and professional activities are health technology assessment, comparative effectiveness, and optimization of drug use. At the Faculty of pharmacy, University of Ljubljana he has built a nationally recognized reference centre for pharmacoeconomic and evidence-based pharmacy practice. Recently, he has served as a member of the Health Council at the Ministry of Health of the Republic Slovenia and as a member of two expert commissions at the Agency for Medicinal Products and Medical Devices of the Republic Slovenia: one focusing on the evaluation of clinical trials and the other on drug prices.
- Assoc. Prof. Igor Locatelli, M Pharm: Igor Locatelli graduated in 2002 at the Faculty of Pharmacy, University of Ljubljana, where he has been employed since 2003. He concluded the postgraduate study of Biomedicine at University of Ljubljana in 2008, when he defended his doctoral thesis in clinical pharmacokinetics. Between 2002 and 2010 he worked as a

researcher within the Department of Biopharmaceutics and Pharmacokinetics, where he was involved in evaluation of pharmacokinetic and statistical models for analysing the data from preclinical studies and clinical trials. In 2010, he joined the Department of Social Pharmacy, since then his research work embraces studies in pharmacoepidemiology and Pharmacoeconomics with an emphasis on meta-analysis of clinical trials.

- Assist. Dr. Nanča Čebron Lipovec, M Pharm: Nanča Čebron Lipovec graduated in 2010 at the Faculty of Pharmacy, University of Ljubljana and started her career as a hospital and clinical pharmacist at the University Clinic of Respiratory and Allergic Diseases Golnik. In 2012, she became a research fellow at the same institution and started her doctoral studies in the field of Social medicine. In 2016 she defended her doctoral thesis on the topic of the effect of nonpharmacological treatment on metabolic profiles in patients with COPD. In 2017 she joined the Department of Social Pharmacy and is now teaching assistant and researcher in the field of pharmacotherapy and pharmacoepidemiology.
- Assist. Prof. Nejc Horvat, M Pharm: Nejc Horvat graduated in 2007 under the supervision of Prof. Dr. Aleš Mrhar and Assist. dr. Mitja Kos. The theme title was Development of a questionnaire measuring patient satisfaction with pharmacy services. In 2014 he defended his doctoral thesis titled: Evaluation of pharmacy services from the patient and expert perspective. Currently, he is a member of different research teams within the Department of Social Pharmacy. His research focus is primarily the outcomes research, particularly evaluation of pharmacy services, health literacy and drug related problems.

Other department members: Assist. Prof. Dr. Lea Knez, M. Pharm., spec.; Assist. Dr. Ana Kodrič, M Pharm, Assist. Dr. Urška Nabergoj Makovec, M. Pharm.; Assist. Dr. Janja Jazbar, M Pharm, Assist. Sara Prelesnik, M. Pharm.

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Country: Netherlands

National Institute for Public Health and the Environment of the Netherlands (RIVM)

Description of the institution (including location): The RIVM is the National Institute for Public Health and the Environment of the Netherlands and has been promoting public health and safeguarding environmental quality for over 100 years. The RIVM has expanded to become a knowledge institute at the centre of Dutch society, advising on health and environment. In our role as trusted advisor, we provide the government with impartial advice on infectious diseases, vaccination, population screening, lifestyle, nutrition, pharmaceuticals, environment, sustainability, and safety. We carry out studies, provide advice and recommendations, and direct and implement prevention and control responses. Our work is primarily commissioned by Dutch ministries and inspectorates and projects are also undertaken within international frameworks, such as the European Union and United Nations. We have many national and international partners and are continuing to build new networks in multidisciplinary cooperation. We are committed to supporting government and society in improving health and the environment.

Description of the research team/researcher(s) involved as to their background, competences, and interests (Country Team NL):

- Teresa Leonardo Alves is currently working as a Researcher for the Health Protection Unit of the National Institute for Public Health and the Environment (RIVM) in Bilthoven, the Netherlands. She holds a Pharm D in Pharmaceutical Sciences from Porto University in Portugal, a Master in Public Health from the Netherlands Institute of Health Sciences (Erasmus University, Rotterdam) and a PhD in Pharmaceutical Policy, Utrecht University, Netherlands. She has more than fifteen years' experience in the coordination and public relations of not-for-profit organizations in the field of pharmaceutical policy, having worked for the *International Pharmaceutical Federation, Health Action International* and the independent bulletin *Prescrire* in a variety of positions covering project management, communications, and policy advocacy. She has developed invaluable knowledge of key stakeholders in European pharmaceutical policy as well as evidence-based advocacy skills. This has required expertise in identifying and maintaining contacts with NGO networks, policymakers, academia, and health authorities. She has also gained extensive experience as a fundraiser, public speaker, event organizer, editor, and coordinator of international studies. From March 2020 to June 2021, she was seconded as Senior Policy Officer at the Ministry of Health, Welfare and Sport in the Netherlands, working on international pharmaceutical policy. At the RIVM, her research has focused on pharmaceutical products and medical devices, covering a wide range of aspects including rational use, shortages, as well as safety and risk minimisation.
- Ingrid Hegger has worked at the National Institute for Public Health and the Environment since 1988. In doing so, she became an expert on the regulation of medicinal products, with special interest in biologicals. From 1990 to 1999 she was the Project Manager for the Control Authority Batch Release of immunological medicinal products and plasma derived products. She also acted as Scientific Assessor of biologicals and was member of the Biological Working Part of the European Medicines Agency from 1995 to 1999. She was also a member of the group of experts Sera and Vaccines of the European Pharmacopoeia, Council of Europe, from 1999 to 2007. Between 2001 and 2006, she was a Project leader for the batch release of investigational medicinal products for clinical trials. From 1999 onwards, her focus shifted towards "close-to-policy" projects in the field of health products, pharmaceutical care, and health policy. Between 2003 and 2006, she was a member of the National working party for the implementation of EU directive 2001/20 on clinical trials. She has been involved in many projects covering a wide variety of topics, among which: existing barriers in the regulation of medicinal products, pharmaco-economics, orphan diseases, advanced medicinal products,

clinical trials, eHealth, pharmacogenomics, pharmaceutical crime, and risk-based supervision. In addition, her Ph.D. focused on the utilization of knowledge within public health policy and healthcare supervision.

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Utrecht University

Description of the institution (including location): The division of Pharmacoepidemiology and Clinical Pharmacology of the Utrecht Institute for Pharmaceutical Sciences contributes to a better understanding of the variability in medicines' use and patient outcomes, both from a clinical, policy and methodological perspective. Despite extensive testing before marketing approval, variability in drug response (both efficacy and safety) is more the rule than the exception when medicines are used in daily clinical practice, i.e., in real life. The research program is inspired by societal needs to ensure that medicines deliver their full therapeutic potential. The program has a systems therapeutics focus, integrating various disciplines, dimensions, and phases of a product life cycle to learn about (rather than confirm) drug effects and their determinants both before and after initial marketing approval of the product. The primary conceptual anchors in the research strategy of the program are Epidemiological Methods, Clinical Pharmacology and Systems Therapeutics. Research is organized into three centers with a strong conceptual research strategy: the Centre for Pharmacoepidemiology, Centre for Clinical Therapeutics, and the Centre for Pharmaceutical Policy and Regulation.

Description of the research team/researcher(s) involved as to their background, competences, and interests (Country Team NL):

- Dr E.R. (Rob) Heerdink PhD is an associate professor of Clinical Pharmacoepidemiology at the Utrecht Institute for Pharmaceutical Sciences, Utrecht University, and professor of Innovation of Pharmaceutical Care at the University of Applied Sciences Utrecht. He is principal investigator and managing director of the Centre for Clinical Therapeutics. His research is driven by questions from clinical practice and spans from traditional pharmaco-epidemiological methods to systems pharmacy research into context related aspects of pharmacotherapy. He has published over 200 peer-reviewed articles on topics including (psychiatric) pharmacotherapy, drug exposure patterns, adherence and the relation between pharmaceutical care and clinical outcomes and has served as co-promotor for over 25 PhD students. Dr Rob Heerdink is a founding and honorary member of the European Society for Patient Compliance and Persistence (Espacomp).
- Dr Shahab Abtahi, MD MSc PhD, is a Postdoctoral Research Fellow at the Division of Pharmacoepidemiology and Clinical Pharmacology at the Utrecht Institute for Pharmaceutical Sciences, Utrecht University. He graduated in 'General Medicine' from Tehran University of Medical Sciences in 2011, obtained a MSc in 'Vitality and Ageing' from Leiden University in 2016 and read his PhD in 'Pharmacoepidemiology' at Maastricht University in 2021. His research is mostly focused on pharmacoepidemiologic studies assessing drugs' effectiveness and safety using electronic healthcare databases, such as the UK Clinical Practice Research Datalink (CPRD), nationwide Danish registries, or Dutch PHARMO Database Network.

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Appendix 1 - Instructions for document search to reconstruct timeline of events at national level

The organization of vaccination campaigns for COVID-19 varies per EU member state. To reconstruct the timeline of events at national level, each national team will conduct an online search for information on their national COVID-19 vaccination campaign. To gather the unindexed information, a snowball strategy will be applied.

For each member state involved, the search depends on the national situation and may include:

- Governmental communications on the COVID-19 vaccination campaign, including press releases and public information on governmental websites.
- Communications from national public health directorates, including press releases and public information on their websites.
- Information from national vaccination authorities, including relevant information on their websites, press releases and any vaccination guidelines.
- Official communications from the national competent authority for medicinal products, including press releases
- Communications from relevant professional organizations (e.g., learned societies for hematologists and GPs)

The timeline will be plotted for the period November 2020 – September 2021. The events regarding the booster campaign for COVID-19 starting in September 2021 will be excluded from this study.

The information collected through snowball approach will be compared with that obtained via the Non-Urgent Information request issued by the EMA to National competent authorities of the Member States involved in this study.

The collated data will provide input to the drafting of the national surveys and to the development of the interview guides.

Appendix 2 - Standard format for collecting information on vaccination policies

A. Vaxzevria: Initial vaccination policy, prior to EMA communication d.d. 29 March 2021

Country	Initial vaccination policy, prior to EMA communication d.d. **29 March 2021**			
	Vaccines used	Target groups	Order of vaccination	Source of information (organization, link to document)
Denmark				
Greece				
Latvia				
Netherlands				
Portugal				
Slovenia				

B. Vaxzevria: Changes in vaccination policy, after EMA communication d.d. 29 March-2021

Country	Initial vaccination policy, after EMA communication d.d. **29 March-2021**				
	Summary change	Vaccines used	Target groups	Prioritisation	Source information
Denmark					
Greece					
Latvia					
Netherlands					
Portugal					
Slovenia					

C. Vaxzevria: Changes in vaccination policy, after EMA communication d.d. 14 April-2021

Country	Initial vaccination policy, after EMA communication d.d. **14 April-2021**				
	Summary change	Vaccines used	Target groups	Prioritisation	Source information
Denmark					
Greece					
Latvia					
Netherlands					
Portugal					
Slovenia					

D. Vaxzevria: Changes in vaccination policy, after EMA communication d.d. 11 May-2021

Country	Initial vaccination policy, after EMA communication d.d. **11 May-2021**			
	Vaccines used	Target groups	Prioritisation	Source information
Denmark				
Greece				
Latvia				
Netherlands				
Portugal				

COVID-19 Vaccine Janssen

A. COVID-19 vaccine Janssen: Initial vaccination policy, prior to EMA communication d.d. 16 April 2021

Country	Initial vaccination policy, prior to EMA communication d.d. **16 April 2021**			
	Vaccines used	Target groups	Order of vaccination	Source information
Denmark				
Greece				
Latvia				
Netherlands				
Portugal				
Slovenia				

B. COVID-19 Vaccine Janssen: Changes in vaccination policy, after EMA communication d.d. 16 April-2021

Country	Initial vaccination policy, after EMA communication d.d. **16 April-2021**				
	Summary change	Vaccines used	Target groups	Prioritisation	**Source information**
Denmark					
Greece					
Latvia					
Netherlands					
Portugal					
Slovenia					

C. COVID-19 vaccine Janssen: Changes in vaccination policy, after EMA communication 22 April 2021

Country	Changes in vaccination policy, after EMA communication d.d. **22 April 2021**				
	Summary change	Vaccines used	Target groups	Prioritisation	Source information
Denmark					
Greece					
Latvia					

Netherlands					
Portugal					
Slovenia					

D. COVID-19 vaccine Janssen: Changes in vaccination policy, after EMA communication d.d. 11 May 2021

Country	Initial vaccination policy, after EMA communication d.d. **11 May-2021**				
	Summary change	Vaccines used	Target groups	Prioritisation	Source information
Denmark					
Greece					
Latvia					
Netherlands					
Portugal					
Slovenia					

Appendix 3 -Translation protocol

Step 1:

Two native speaking researchers (or translators) translate the documents separately i.e., they translate the citizen's questionnaire, the healthcare professional's questionnaire, or the interview guide in tandem. This process results in individually translated versions of the 2 questionnaires and one interview guide from the two translators.

Step 2:

The two translators then meet, compare, and discuss the wording of each question in their individual versions for each of the questionnaires or the interview guide.

During this process they focus on:

- The target group for the questionnaires and their use of words and specific terms
- How citizens as lay persons use words and terms about medicines and health
- Consistency of wording throughout all questionnaires, although citizen's questionnaire will differ in wording from questionnaires for professionals
- Keeping the wording as simple as possible

This process results in the one consensus version for each of the 2 translated questionnaires or for the interview guide.

Step 3:

Then a third native speaking researcher (or validator), who is also a healthcare professional and has not seen the questionnaires before and is not familiar with the study, reads the agreed-upon version of the translated questionnaires or the interview guide, raising questions and noting any lack of clarity, which are then to be clarified during a meeting with the two translators.

This process results in the validated versions of the 2 translated questionnaires or in the validated interview guide.

Step 4:

The validated versions of the 2 translated questionnaires or the interview guide are then compared to their corresponding English versions and any remaining inconsistencies are resolved by consensus between the two translators and the validator.

This process results in the final versions of the 2 translated questionnaires or in the final interview guide.

Appendix 4 – Draft Questionnaire for Citizens

(The text in green refers to items included in the research plan. These will not be included in the final questionnaire)
(The text in blue offers instructions (to skip questions) or additional information for national coordinators. The general rule is selecting one response per question, unless indicated otherwise)

We are conducting an international survey on behalf of the European Medicines Agency (EMA) to monitor how the public across the European Union is being informed about the safety of certain vaccines.

This is an international study, which includes research centres across six European Member States. In

(Include country) this research is being led in by (Include name of centre).

Our study concerns the safety of COVID-19 vaccines.

You are invited to fill in this questionnaire as you were contacted to be vaccinated or have received a COVID-19 vaccine. We are particularly interested in knowing more about the information you have received about the vaccine and how that might have influenced your decisions.

We estimate that it will take 10 to 15 minutes to answer the questions below. The information provided will inform the European Medicines Agency and contribute to improve future guidance to the public about the use and safety of COVID-19 vaccines.

The data will be treated confidentially and will not be associated with you personally. Answers will be registered anonymously and handled in accordance with the General Data Protection Regulation (or GDPR) (EU) 2016/679 of 27 April 2016.

Your participation is voluntary. You can also stop at any time while completing the questionnaire. The questionnaire contains questions about your health and whether you have been vaccinated. These are special personal data. **By replying, you are expressly consenting for this data to be used for research purposes.**

- o I hereby declare to have read and understood the information provided above and accept free-willingly to participate.

- o I would like to receive information about the results of this study by e-mail. Please provide your e-mail_____

Baseline characteristics

(1) Respondent characteristics: age, gender, belonging to a risk group for COVID-19 and/or a professional group with vaccination priority according to the national vaccination policy.

Age

Q1a. What is your year of birth?

- Year _ _ _ _

Gender

Q1b. What is your gender?

- Male
- Female
- Other
- I would rather not say

Belonging to a risk group for COVID-19i

Q1c. Do you suffer from one or more of the following underlying health conditions? (List of conditions is provided; respondents can select conditions and answer. Countries can adapt list as needed/relevant)

- Chronic respiratory disease or lung problems
- Chronic heart disease
- Diabetes (diabetes mellitus)
- Severe kidney disease leading to dialysis or kidney transplantation
- HIV infection
- Severe liver disease
- Very severe overweight (BMI over 40) [Information bar: The BMI (Body Mass Index) is an estimate of the health risk of your body weight. BMI is calculated based on a person's weight and height.]
- Lower resistance to infection:
- Due to medication for autoimmune diseases
- Following organ or stem cell transplantation
- Due to a non-functioning or missing spleen
- Due to blood disease
- Due to severe immune disorders requiring treatment
- Due to chemotherapy and/or radiation for cancer
- Due to medication that lowers your ability to resist an infection
- No
- I would rather not say

Belonging to a professional group with vaccination priority according to the national vaccination policy

Q1d. Do you belong to a professional group with vaccination priority?

- Healthcare Professional
- Care staff (nursing home, hospital staff)
- Military
- Emergency response services
- Educational staff (scholars, school staff)
- Government
- Other, please explain [Open answer] _____

Q1e. What is the highest level of education that you have completed?

- Primary school
- Secondary school
- Professional school
- University, undergraduate
- University, postgraduate
- Other, please explain. [Open answer] _____

[Information bar: By "vaccination against the coronavirus" we mean a vaccination with one of the vaccines that were approved for the (Include country) market until June 2021. These were:

- Comirnaty (developed by BioNTech and Pfizer)
- Spikevax (previously COVID-19 Vaccine Moderna)
- Vaxzevria (previously COVID-19 Vaccine AstraZeneca)
- COVID-19 Vaccine Janssen]

(2) Date at which they were invited for vaccination.
(3) Present status of vaccination against COVID-19 and period of first and second vaccination.
(4) Vaccine received

[National teams can decide whether to include Q2a and Q2e in their questionnaires or not]

Q2. Have you been vaccinated against the new coronavirus?

- No [go to question Q2a]
- Yes, I have had one jab against the coronavirus [go to question Q2b, then Q3]
- Yes, I have had two jabs against the coronavirus [go to question Q2b, then Q2d, then Q3]
- Yes, I have had three jabs against the coronavirus [go to question Q2b, then Q2d, then 2d, then Q3]

Q2a. What were the main reasons for you not to get vaccinated?

- I was concerned about the side effects.
- I do not trust these vaccines which have not been sufficiently tested.
- Authorities are pushing excessively to get the population vaccinated.
- It infringes on my civil rights.
- In my view COVID-19 is not a dangerous disease.
- Other, please explain. [Open answer] _____

[go to question Q5]

Q2b. When did you receive your first jab against the coronavirus?
(Insert dropdown menu with all the months in 2021 and January to May 2022)

- Jan, Feb, Mar, Apr, May, Jun, Jul, Aug, Sep, Oct, Nov, Dec - 2021
- Jan, Feb, Mar - 2022
- I do not recall.

Q2b.a. Which vaccine did you receive?

- Comirnaty (developed by BioNTech and Pfizer)
- Spikevax (previously COVID-19 Vaccine Moderna)
- Vaxzevria (previously COVID-19 Vaccine AstraZeneca) [go to question Q5]
- COVID-19 Vaccine Janssen] [go to question Q5]
- I do not recall

Q2c. When did you receive your second jab against the coronavirus?
(Insert dropdown menu with all the months in 2021 and January to May 2022)

- Jan, Feb, Mar, Apr, May, Jun, Jul, Aug, Sep, Oct, Nov, Dec -2021
- Jan, Feb, Mar, April, May 2022
- I do not recall.

Q2c.a. Which vaccine did you receive?

- Comirnaty (developed by BioNTech and Pfizer)
- Spikevax (previously COVID-19 Vaccine Moderna)
- Vaxzevria (previously COVID-19 Vaccine AstraZeneca) [go to question Q5]
- COVID-19 Vaccine Janssen] [go to question Q5]
- I do not recall

Q2d. When did you receive your third jab against the coronavirus?
(Insert dropdown menu with all the Q3 and Q4 in 2021 + Q1 and Q2 2022)

- Sep, Oct, Nov, Dec -2021
- Jan, Feb, Mar, April, May 2022
- I do not recall.

Q2d.a. Which vaccine did you receive?

- Comirnaty (developed by BioNTech and Pfizer)
- Spikevax (previously COVID-19 Vaccine Moderna)
- Vaxzevria (previously COVID-19 Vaccine AstraZeneca) [go to question Q5]
- I do not recall

Q3. What were the main reasons for you to get vaccinated?

- To avoid becoming ill with COVID-19.
- To protect family and friends from becoming ill with COVID-19.
- To prevent the spread of coronavirus in society.
- Other, please explain [Open answer]

_____

[go to question Q4]

[Information bar: By "vaccination against the coronavirus" we mean a vaccination with one of the vaccines that were approved for the (Include country) market until June 2021. These were:

- Comirnaty (developed by BioNTech and Pfizer)
- Spikevax (previously COVID-19 Vaccine Moderna)
- Vaxzevria (previously COVID-19 Vaccine AstraZeneca)
- COVID-19 Vaccine Janssen]

(5) Awareness and perceptions about the benefits and risks of the SARS-CoV-2 adenovirus vector vaccines.

Q4. Are you aware that like all medicines, the COVID-19 vaccines can cause side effects?

- Yes
- No
- Not sure

(6) Awareness and perceptions about the risk for TTS from adenovirus vaccines.

Q5. There have been reports of extremely rare cases of blood clots with low platelets in people who had received the Oxford/AstraZeneca vaccine or the Janssen vaccine, particularly women under 60 years of age. Were you aware of this side effect?

- Yes. If so, when?
    - Before my first dose [go to question Q5b, then Q6]
    - Before my second dose [go to question Q5b, then Q6]
    - Before my third dose [go to question Q5b, then Q6]
- No
- Not sure

Q5a. Please select from the list below, to the best of your knowledge, the signs and/or symptoms of blood clots with low platelets (Select all that apply):

- a severe headache that is not relieved with painkillers or is getting worse
- a headache that feels worse when you lie down or bend over
- a headache that is unusual along with blurred vision, feeling or being sick, problems speaking, weakness, drowsiness, or seizures (fits)
- a rash that looks like small bruises or bleeding under the skin
- shortness of breath, chest pain, leg swelling or persistent abdominal pain
- nausea
- pain or swelling at the injection site.

(7) Source of information about the risk for TTS.

Q6. Where did you learn about the rare cases of blood clots with low platelets triggered by some COVID-19 vaccines? (Choose all that apply)

- I was informed by a General Practitioner
- I was informed at the vaccination centre
- I was informed at the pharmacy
- I was informed by a Specialist Physician
- I filled in a medical history form and became aware of this risk
- I heard about it from mainstream media (TV, radio, newspapers)
- I found information on the Internet (e.g., news portals or social media such as Facebook, LinkedIn, Twitter, Facebook, or Instagram)
- I read the package leaflet / patient information leaflet
- I heard about it during my professional activity as a healthcare professional
- Just now, when filling in this questionnaire.
- Other, please explain: [Open answer] _____

(8) Awareness about changes in COVID-19 vaccination policy and their impact on own perceptions and attitudes regarding vaccination against COVID-19.

(Country specific timeline of events is inserted, indicating the period and communications we are asking about)

Q7. Has your willingness to receive the Vaxzevria vaccine or the COVID-19 Vaccine Janssen changed since you heard about their association with blood clotting risks?

- Not at all, it did not change
- I am not sure
- Yes, it changed.

Q8. Has your willingness to receive any COVID-19 vaccination been altered since there were changes to the national COVID-19 vaccination programme due to the side-effects associated with the Astra Zeneca and the Janssen vaccines?

- Not at all, it did not change
- I am not sure
- Yes, it changed.

Q9. Has your willingness to receive the Vaxzevria vaccine or the COVID-19 Vaccine Janssen been altered since there were changes to the national COVID-19 vaccination programme due to their side-effects?

- Not at all, it did not change
- I am not sure
- Yes, it changed.

(9) Changes to own attitudes towards vaccination against COVID-19 and use of COVID-19 vaccines: no vaccination, postponement of vaccination, decision to change vaccine.

[If yes to Q7 and/or yes to Q8 and/or yes to Q9, then go to Q10]

Q10. Could you please describe how your attitudes changed? Did you:

- Choose not to get vaccinated. Why? [Open answer] _____
- Postpone vaccination. Why? [Open answer] _____
- Ask to change the choice of vaccine beforehand or at an appointment [go to question Q9b]
- Other, please explain. [Open answer] _____

Q10a. What prompted your decision to change the vaccine? [Open answer]

_____
_____
_____

Q10b. Could you please briefly describe...

- You asked to change the vaccine
  - (Before or) at the first dose/jab appointment
  - (Before or) at the second dose/jab appointment
- The vaccine attributed was...
  - Comirnaty (developed by BioNTech and Pfizer)
  - Spikevax (previously COVID-19 Vaccine Moderna)
  - Vaxzevria (previously COVID-19 Vaccine AstraZeneca)
  - COVID-19 Vaccine Janssen
- You asked to change to...
  - Comirnaty (developed by BioNTech and Pfizer)
  - Spikevax (previously COVID-19 Vaccine Moderna)
  - Vaxzevria (previously COVID-19 Vaccine AstraZeneca)
  - COVID-19 Vaccine Janssen

Q10c. Were you successful in changing the vaccine(s)?

- Yes
- No. Please explain why not_____

(10) Changes to own attitudes towards potential vaccination of their young adult-teenager children against COVID-19.

Q11. Do you have any offspring between 5 and 18 years of age?

- Yes, please select all that apply:
    - Younger than 5 years of age [go to question Q10a]
    - Aged between 5 and 12 years of age [go to question Q10a]
    - Older than 12 years [go to question Q10a]
- No

Q11a. Have your children – aged between 5 and 18 – been vaccinated against COVID-19?

- Yes, my children have had the recommended vaccination [go to question Q11b]
- Yes partially, my children have not had all the vaccinations recommended for their age [go to question Q11b]
- No, my children are not vaccinated against COVID-19. [go to question Q11c]
- I would rather not say

Q11 b. What were the main reasons to get your children vaccinated against COVID-19?

- To avoid that they would become ill with COVID-19.
- To protect family and friends from becoming ill with COVID-19.
- To prevent the spread of coronavirus in society.
- Other, please explain. _____

Q11 c. What were the main reasons for not vaccinating your children aged between 5 and 18 against COVID-19?

- I was concerned about the side effects.
- I do not trust these vaccines which have not been sufficiently tested.
- Authorities are pushing excessively to get the population vaccinated.
- It infringes on my civil rights.
- In my view COVID-19 is not a dangerous disease.
- Other, please explain. [Open answer] _____

(11) Changes to own attitudes towards vaccination programmes in general.

INSTRUCTIONS: These questions have a series of answers with two extreme or opposite possibilities. For instance, 'don't agree at all' versus 'totally agree'. The middle option is considered neutral. On the answer scale, please indicate which option best matches your opinion or situation.

We would like to learn more about your views relating to the widespread use of vaccines to prevent diseases. Please select the option which applies to you:

Q12. I find that using vaccines to prevent disease in general is…						
	1	2	3	4	5	
Not important						Important
Unsafe						Safe
Imprudent						Prudent

[Information bar: By "vaccination against the coronavirus" we mean a vaccination with one of the vaccines that are currently approved for the (Include country) market. These are the following vaccines:

- BioNTech/Pfizer
- Moderna
- AstraZeneca
- Janssen]

Q13. I find that using vaccines to prevent COVID-19 is...						
	1	2	3	4	5	
Not important						Important
Unsafe						Safe
Imprudent						Prudent

(12) Changes to own attitudes towards general children vaccination programmes.

In (Include country) children can follow the national childhood vaccination programme. These vaccines aim to protect children against infectious diseases. What is your opinion about it?

Q14. I find the national childhood vaccination programme to be…						
Unnecessary						Necessary
Unacceptable						Acceptable
Safe						Unsafe
Good						Bad
Unclear						Clear

Q14a. Are your children under 18 years of age vaccinated according to the national childhood vaccination programme of (Include country)?

- Yes, my children have had all the recommended vaccinations
- Yes partially, my children have some of the vaccinations recommended for their age
- No, my children are not vaccinated according to the national childhood vaccination programme.
- I would rather not say

(13) Willingness to receive future (booster) vaccination(s) against COVID-19.

Q15. Have the reports about the side-effects associated with the Astra Zeneca and the Janssen vaccines influenced your willingness to receive booster vaccinations against COVID-19, either recently or in the future?

- Not at all, they did not change my views on recent or future vaccination against COVID-19.
- They changed my views but not my willingness to be vaccinated
- Yes, they changed my views and willingness to be vaccinated. [go to question Q13b]
- I am not sure.

Q15a. Could you please explain what has changed? Did you:

- Choose not to get a booster. Why? [Open answer] _____
- Postpone booster vaccination. Why? [Open answer] _____
- Other, please explain [Open answer]. _____

(Country specific timeline of events is inserted, indicating the period and policy changes we are asking about)

Q16a. Have the changes to the COVID-19 vaccination programmes affected your willingness to receive booster vaccinations against COVID-19 in the future?

- Not at all, they did not change my views on recent or future vaccination against COVID-19.
- They changed my views but not my willingness to be vaccinated
- Yes, they changed my views and willingness to be vaccinated. [go to question Q14b]
- I am not sure.

Q16b. Could you please describe what has changed? Did you:

- Choose not to get a booster. Why? [Open answer] _____
- Postpone booster vaccination. Why? [Open answer] _____
- Other, please describe. [Open answer] _____

Q17. Due to the reports about the side-effects associated with the Astra Zeneca and the Janssen vaccines…							
…I am less likely to get vaccinated against COVID-19 in the future	Disagree completely	1	2	3	4	5	Agree Completely
…I feel less safe about getting vaccinated against COVID-19	Disagree completely	1	2	3	4	5	Agree Completely

Q18. Due to the changes in the national vaccination programme for COVID-19 …							
…I am less likely to get vaccinated against COVID-19 in the future	Disagree completely	1	2	3	4	5	Agree Completely
…I feel less safe about getting vaccinated against COVID-19	Disagree completely	1	2	3	4	5	Agree Completely

Thank you very much for your participation!

Appendix 5 – Draft Questionnaire for Healthcare Professionals

(Text in green refers to issues mentioned in the research plan to make sure all these issues are covered, it will not appear in the questionnaire)
(Text in blue refers to **skip patterns** and other instructions for national coordinators)

Dear Healthcare Professional,

As you are certainly aware, the knowledge about a medicine is not only built up during its research and development stages, but also once it is available on the market and being used by a larger group of patients. We are conducting an international survey funded by the European Medicines Agency (EMA) to monitor how information about the safety of SARS-CoV-2 vaccines has been conveyed to healthcare professionals and citizens, across the European Union.

This is an international study, which includes research centres across six European Member States. In (Include country) this research is being led in by (Include name of centre).

Our study concerns the use of adenovirus vector vaccines against SARS-CoV-2. Below is a list of vaccines approved to be used in (include country): <insert trade names for the available vaccines>

You are invited to fill in this questionnaire. We are particularly interested in knowing more about the information you have received about these vaccines and how that might have influenced your practice and the guidance you have provided to the public/patients in the past and will be providing in the future.

We estimate that it will take 10 to 15 minutes to answer the questions below. The information from this study will inform the European Medicines Agency pharmacovigilance activities and will contribute to increased knowledge about how to better advise healthcare professionals and the public about the safety of vaccines.

Your participation is voluntary. Answers will be registered anonymously and handled in accordance with the General Data Protection Regulation (or GDPR) (EU) 2016/679 of 27 April 2016.

□ I hereby declare to have read and understood the information provided above and accept free-willingly to participate. I allow my response to be recorded and analysed by the researchers.

□ I would like to receive information about the results of this study by e-mail. Please provide your e-mail_____

Baseline characteristics

Q1a. What is your year of birth?
- Year _ _ _ _

Q1b. What is your gender?
- Male
- Female
- Other
- I would rather not say

Q1c. What is your current profession?

- Physician, General Practitioner/Family doctor
- Physician, Specialist (Haematology)
- Physician, Specialist (Internal Medicine)
- Physician, Specialist (Vascular Surgery)
- Nurse
- Pharmacist
- Veterinarian
- Other, please specify _____

Q1d. How long have you practiced in your current field?
- 0-5 years
- 6-10 years
- 11-20 years
- 21-30 years
- 31 years or longer

Q2. Were you actively involved in the vaccination programme, administering vaccines, treating adverse effects, or providing guidance to the public/patients about the risks associated with the SARS-CoV-2 vaccination?
- Yes **[go to question Q3a]**
- Never.
- I am not sure

If "Never," the respondent is thanked, and the survey stops here.
Message: Thank you for your interest in participating but given that you have not been actively involved in the vaccination against SARS-CoV-2 nor providing advice thereover, your input is outside the scope of this study.

(1) HCP's own working/vaccination duty context (vaccination centres, own medical practice, hospital).

Q3a. Where were you involved in the vaccination against SARS-CoV-2, in the provision of advice thereover or in the treatment of side-effects from vaccination? (Select all that apply):
- Dedicated vaccination centre
- Primary Care practice
- Hospital practice
- Pharmacy
- Dedicated healthcare phone information service **(each country is to add its specific name)**
- Other, please specify _____

Q3b. On average, how often were you involved either vaccinating or providing advice about COVID-19 vaccines or treating adverse reactions to COVID-19 vaccination throughout 2021?
- Daily
- Once a week or more
- 2-3 times per month
- Once a month or less frequently
- Other, please specify _____

(2) How they became aware of TTS (through media, professional society, direct healthcare communication, SmPC, instructions from authorities

Q4. There have been reports of extremely rare cases of thrombosis with thrombocytopenia (blood clots with low platelets) in people who had received the Vaxzevria or the COVID-19 Vaccine Janssen. Are you aware of that?

- Yes **[go to question Q4b]**
- No
- Not sure

(Please adjust the timelines included in question 4b below to reflect your country's timeline, bearing in mind the period during which your local competent authorities implemented the measures established by the EMA)

Q4a. When did you learn about the reports of thrombosis with thrombocytopenia syndrome (TTS) associated with SARS-CoV-2 adenovirus vector vaccines?

- January to April 2021. **go to Q4c.**
- May to August 2021. **go to Q4c.**
- September to December 2021. **go to Q4c.**
- January 2022 until now. **go to Q4c.**
- Just now, when answering this questionnaire

Q4b. Where did you obtain that information? (Choose all that apply)

- Health authorities
- Drug Regulatory Agencies
- Professional societies
- Colleagues
- Mainstream Media (TV, radio, newspapers)
- Professional or scientific journals
- Manufacturers (e.g., printed, or electronic materials)
- Internet (social media, Facebook, LinkedIn, news portals)
- Symposia or conferences
- During academic studies
- During post-academic training/continuous professional education
- Other, please specify: _____

(3) Whether they received and were aware of the direct healthcare professional communications (DHPCs).

Q5a. I have vaccinated or provided advice about the following SARS-CoV-2 vaccines (Select all that apply):

- Comirnaty (developed by BioNTech and Pfizer) **(go to Q7a)**
- Spikevax (previously COVID-19 Vaccine Moderna) **(go to Q7a)**
- Vaxzevria (previously COVID-19 Vaccine AstraZeneca) **(go to 5b).**
- COVID-19 Vaccine Janssen **(go to 5c).**

Q5b. Think about **the last time you vaccinated a patient with** Vaxzevria **or provided advice about this vaccine**. Did you apply any of the measures described below, which were established in 2021? (One option to be chosen per row)

		Yes, I did it	I have seen it but did use it	No, I have never seen/used it	I am not sure
Q5b.a	Consult the Summary of Product Characteristics* (Please click the link to see an example)	1.1	1.2	1.3	1.4
Q5b.b	Consult the Package Leaflet/Patient Information Leaflet* (Please click the link to see an example)	2.1	2.2	2.3	2.4
Q5b.c	Consult the Direct Healthcare Professional Communication letter* (Please click the link to see an example)	3.1	3.2	3.3	3.4
Q5b.d	Consult the Guidance* from the national health authority (add name according to country) (Please click the link to see an example)	4.1	4.2	4.3	4.4

*Clicking on the link opens an explanation with a visual example of the specific measure used in the country

** Each country adapts (leaves or deletes what is in the brackets) depending on the country situation

All the answers are registered first, then:
Consider Q5b.a first, and for those who did not tick 1.1 (i.e., tick 1.2, 1.3, 1.4) insert Q5b.aa, and then move to the next questions that follows
Then consider Q5b.b, and for those who did not tick 2.1 (i.e., tick 2.2, 2.3, 2.4) insert Q5b.ab, and then move to the next questions that follows
Then consider Q5b.c, and for those who did not tick 3.1 (i.e., tick 3.2, 3.3, 3.4) insert Q6c, and then move to the next questions that follows
Then consider Q5b.d, and for those who did not tick 4.1 (i.e., tick 4.2, 4.3, 3.4) insert Q6c, and then move to the next questions that follows

Q5b.aa. In the future, how likely are you to consult the "Summary of Product Characteristics" * before immunising or consulting individuals who are to be immunised with **Vaxzevria**?

- Very unlikely
- Unlikely
- Neither unlikely nor likely
- Likely
- Highly likely

If "Very unlikely" or "Unlikely," go to Q5b.aa_ad

Q5b.aa_ad. Please explain why not_____

Q5b.ab. In the future, how likely are you consult the “Package Leaflet” * when immunising or consulting individuals who are to be immunised with **Vaxzevria**?

- Very unlikely
- Unlikely
- Neither unlikely nor likely
- Likely
- Highly likely

If “Very unlikely” or “Unlikely,” go to Q5b.ab_ad

Q5b.ab _ad. Please explain why not_____

Q5b.ac. In the future, how likely are you to consult the “Direct Health Professional Communication” * regarding vaccination against COVID-19?

- Very unlikely
- Unlikely
- Neither unlikely nor likely
- Likely
- Highly likely

If “Very unlikely” or “Unlikely,” go to Q5b.ac_ad

Q5b.ac_ad. Please explain why not_____

Q5b.ad. In the future, how likely are you to consult the National guidelines * regarding vaccination against COVID-19?

- Very unlikely
- Unlikely
- Neither unlikely nor likely
- Likely
- Highly likely

If “Very unlikely” or “Unlikely,” go to Q5b.ad_ad

Q 5b.ad _ad. Please explain why not_____

Q5c. Think about **the last time you vaccinated a patient with the COVID-19 Vaccine Janssen or provided advice about this vaccine**. Did you apply any of the measures described below, which were established in 2021? (One option to be chosen per row)

(Country specific timeline of events is inserted, indicating the period and communications we are asking about)

		Yes, I did it	I have seen it but did use it	No, I have never seen/used it	I am not sure
Q5c.a	Consult the Summary of Product Characteristics* (Please click the link to see an example)	1.1	1.2	1.3	1.4
Q5c.b	Consult the Package Leaflet/Patient Information Leaflet* (Please click the link to see an example)	2.1	2.2	2.3	2.4
Q5c.c	Consult the Direct to Healthcare Professional Communication letter* (Please click the link to see an example)	3.1	3.2	3.3	3.4
Q5c.d	Consult the Guidance* from the national health authority (add name according to country) (Please click the link to see an example)	4.1	4.2	4.3	4.4

*Clicking on the link opens an explanation with a visual example of the specific measure used in the country

** Each country adapts (leaves or deletes what is in the brackets) depending on the country situation

All the answers are registered first, then:
Consider Q5c.a first, and for those who did not tick 1.1 (i.e., tick 1.2, 1.3, 1.4) insert Q5c.aa, and then move to the next questions that follows
Then consider Q5c.b, and for those who did not tick 2.1 (i.e., tick 2.2, 2.3, 2.4) insert Q5c.ab, and then move to the next questions that follows
Then consider Q5c.c, and for those who did not tick 3.1 (i.e., tick 3.2, 3.3, 3.4) insert Q5c.ac, and then move to the next questions that follows
Then consider Q5c.d, and for those who did not tick 4.1 (i.e., tick 4.2, 4.3, 3.4) insert Q5c.ad, and then move to the next questions that follows

Q5c.aa. In the future, how likely are you to consult the "Summary of Product Characteristics" * before immunising or consulting individuals who are to be immunised with **the COVID-19 Vaccine Janssen**?

- Very unlikely
- Unlikely
- Neither unlikely nor likely
- Likely
- Highly likely

If "Very unlikely" or "Unlikely," go to Q5c.aa _ad

Q5c.aa _ad. Please explain why not_____

Q5c.ab. In the future, how likely are you consult the "Package Leaflet" * when immunising or consulting individuals who are to be immunised with **Vaxzevria**?

- Very unlikely
- Unlikely
- Neither unlikely nor likely
- Likely
- Highly likely

If "Very unlikely" or "Unlikely," go to Q5c.ab_ad

Q5c.ab _ad. Please explain why not_____

Q5c.ac. In the future, how likely are you to consult the "Direct Health Professional Communication" * regarding vaccination against COVID-19?

- Very unlikely
- Unlikely
- Neither unlikely nor likely
- Likely
- Highly likely

If "Very unlikely" or "Unlikely," go to Q5c.ac_ad

Q5c.ac_ad. Please explain why not_____

Q5c.ad. In the future, how likely are you to consult the National guidelines * regarding vaccination against COVID-19?

- Very unlikely
- Unlikely
- Neither unlikely nor likely
- Likely
- Highly likely

If "Very unlikely" or "Unlikely," go to Q5c.ad_ad

Q 5c.ad _ad. Please explain why not_____

(4) Whether they have witnessed any TTS cases in their vaccination practice.

Q6. In your practice, have you ever suspected or witnessed TTS in adults, that may have been associated with the administration of Vaxzevria or with the COVID-19 Vaccine Janssen?

- Yes. What did you do (Select all that apply)?
  - Treat the patient.
  - Referred the patient to a specialist physician.
  - Other, please explain_____
- No
- I am not sure

(5) Knowledge and awareness of the signs and symptoms of TTS and the need to refer to specialists (e.g., haematologists, specialists in coagulation) to diagnose and treat the

condition; any instructions from vaccination authorities and/or national competent authorities for medicinal products and/or clinical practice guidelines when coming across TTS (depending on country).

Q7a. In your opinion, those at greater risk of developing TTS after vaccination with **Vaxzevria or with the COVID-19 Vaccine Janssen** are … (Select all that apply):

- Women under 60 years old
- Men under 60 years old
- People older than 60 years
- Patients with history of thromboembolic events
- Patients with history of cardiovascular events
- Other, please explain_____

Q7b. Please select from the list below the signs and/or symptoms of TTS (Select all that apply):

- a severe headache that is not relieved with painkillers or is getting worse
- a headache that feels worse when you lie down or bend over
- a headache that is unusual along with blurred vision, feeling or being sick, problems speaking, weakness, drowsiness, or seizures (fits)
- a rash that looks like small bruises or bleeding under the skin
- shortness of breath, chest pain, leg swelling or persistent abdominal pain
- nausea
- pain or swelling at the injection site.

(8) Knowledge and awareness of (updated) clinical guidelines and recommendations from learned societies for treating TTS (e.g., with anticoagulants) when available/applicable.

Q7c. Did you receive any instructions about what to do if you suspect a case of thrombosis in combination with thrombocytopenia after vaccination with **Vaxzevria or with the COVID-19 Vaccine Janssen**?

- Yes. (Go to Q7d)
- No
- I am not sure

Q7d. From whom did you receive instructions about what to do if you suspect a case of thrombosis in combination with thrombocytopenia after with Vaxzevria or with the COVID-19 Vaccine Janssen?

- From health authorities
- From national competent authorities for medicinal products
- From clinical practice guidelines
- From recommendations to treat TTS established by learned societies
- Scientific journals

(6) Whether they have informed citizens about the TTS warning signs/symptoms and urged them to seek further health assistance should they occur.

(7) Knowledge and awareness of the contraindications to use adenovirus vector vaccines in patients who have experienced TTS following vaccination with Vaxzevria.

We want to know more about the advice you provided about side-effects from vaccination and their monitoring.

Q8a. Please indicate the option that best describes your behaviour, after the implementation of measures in 2021 (choose one option per row)
(Country specific timeline is inserted, with an arrow indicating the exact period we are asking about)

		Strongly Agree	Somehow agree	Somehow disagree	Strongly Disagree	Not relevant to me
	Vaccination					
Q8aa	I inform citizens about the importance of monitoring health symptoms after vaccination.					
Q8ab	I inform citizens about TTS symptoms and the importance of monitoring them after vaccination.					
Q8ac	I do not administer Vaxzevria or COVID-19 Vaccine Janssen to individuals who were at higher risk of developing TTS.					
Q8ad	When vaccinating, I advise patients to seek further assistance should warning signs occur after Vaxzevria or the COVID-19 Vaccine Janssen.					
Q8ae	I do not use Vaxzevria in patients who had previously experienced TTS following vaccination with Vaxzevria					
	Monitoring Side-effects					
Q8af	I am alert to the signs and symptoms of thromboembolism and or thrombocytopenia.					
Q8ag	I actively check for signs of thrombosis or refer to a specialist those patients who are diagnosed with thrombocytopenia within 3 weeks after					

	vaccination with Vaxzevria or with the COVID-19 Vaccine Janssen.					
Q8g	I actively investigate for signs of thrombocytopenia or refer to a specialist those patients who had a thrombosis within 3 weeks of vaccination with Vaxzevria or with the COVID-19 Vaccine Janssen.					

(8) Whether and how the TTS risk communication has affected their attitudes towards the COVID-19 vaccination campaign and national vaccination programme in general.

(Country specific timeline of events is inserted, indicating the period and communications we are asking about)

Q9. Which communications or materials updated issued in 2021 for **Vaxzevria and the COVID-19 Vaccine Janssen** have had impact on your vaccination patterns and counselling to the public? (Please select all that apply)

- Updates to Summary of Product Characteristics
- Updates to Package Leaflet/Patient Information Leaflet.
- Direct to Healthcare Professional Communication letter*
- Updates to Guidelines/Guidelines from Health Authorities
- Recommendations from professional bodies
- None of the above, there was no impact.

(Country specific timeline of events is inserted, indicating the exact period we are asking about)

Q10. Have your provision of information/counselling/vaccination practice changed since the implementation of measures for established in 2021 by the European Medicines Agency for **Vaxzevria and for the COVID-19 Vaccine Janssen (**i.e. (Updates to Summary of Product Characteristics, Update to the Package Leaflet/Patient Information Leaflet, Direct to healthcare professional communication letter*)?

- Not at all
- Probably not
- Not sure
- Probably yes
- Certainly yes

If "Probably yes" or "Certainly yes" go to Q10a.

Q10a. Please describe briefly how your provision of information/counselling/vaccination practice has changed as a result of the warning about TTS?

_____
_____
_____
_____

(9) Identifying barriers preventing the implementation of regulatory recommendations

Q11. Are there any barriers hindering the implementation and/or use of the communication measures established in 2021 by the European Medicines Agency (Updates to Summary of Product Characteristics, Update to the Package Leaflet/Patient Information Leaflet, Direct to healthcare professional communication letter*) in your country?

- Yes. Please include at least one example. _____
- No.

Q12. Are there any additional points/suggestions/concerns you would like to raise, in what concerns the administration/ implementation of vaccines against COVID-19 and the counselling about their potential risks?

_____
_____
_____
_____
_____
_____

Thank you for participating!

Appendix 6 -Pointers for Interview guide with Healthcare Professionals

According to the study protocol:

"Deeper insight into the knowledge, attitude and perceptions of HCPs will be gained by conducting semi-guided (telephone or online) interviews.

The interviews with healthcare professionals will provide other in-depth information about how HCPs have perceived the timeline of events and the risk communication about the two adenovirus vector vaccines in their country. (Principle #1)

They will also be invited to reflect about their experiences, attitudes, and behaviour. (Principle #2)

Special attention will be paid to scope professionals' motivations and beliefs towards COVID-19 vaccination. (Principle #3)

The interviews will provide details about personal views, which cannot be obtained through the survey. Since HCPs play a crucial role in reassuring and informing people about vaccinations, their perceptions about the risk communication will provide the Pharmacovigilance Risk Assessment Committee with greater insight into the impact of its recommendations in actual practice, as well as help explain any country differences."

			Principle
Information provided on TTS risk associated with adenovirus COVID-19 vaccines	**Information FORMAT**	**Adequate language/format?**	**#1**
		Suggestions?	
	Information CONTENT	**Adequate/Clear/Complete?**	**#1**
		Suggestions?	
	Information CHANNEL	**Adequate/Accessible?**	**#1**
		Suggestions?	
	Information SENDER	**Adequate/Credible/Reliable?**	**#1**
		Importance of National Competent Authorities/health and regulatory authorities?	**#1**
		Suggestions?	
	Information IMPACT	**Understanding the risk**	**#1**
		Understanding who is at risk	**#1**
		Understanding which signs/symptoms should be monitored	**#1**
		Understanding which measures should be taken by HCPs	**#2**
		Affecting confidence/fear in vaccines	**#3**
		Attitudes/Behaviour changes **Brand switching advice** **Vaccination refusal advice**	**#2**
		Comments	