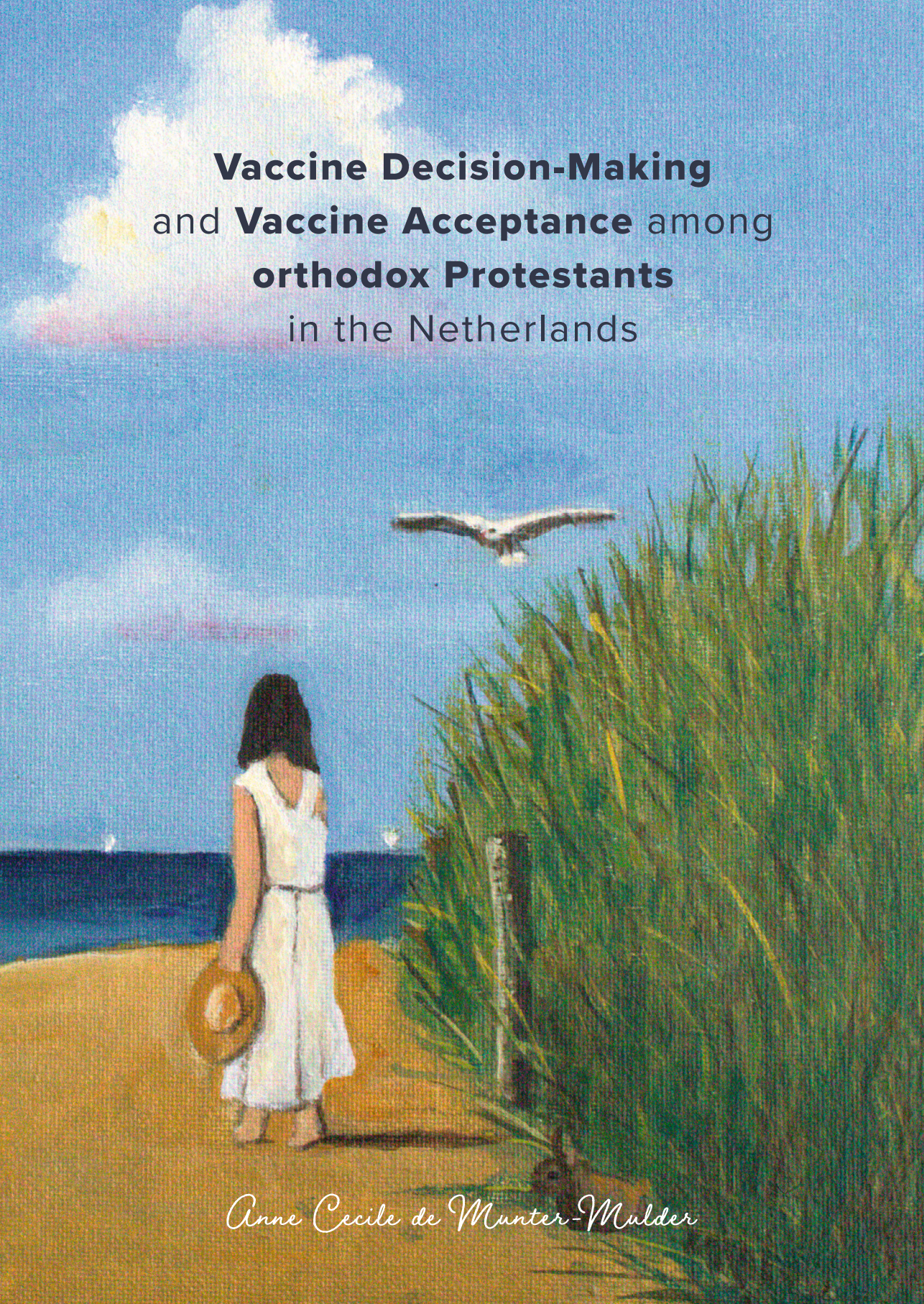
Vaccine Decision-Making and **Vaccine Acceptance** among **orthodox Protestants** in the Netherlands



Anne Cecile de Munter-Mulder

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ISBN: 978-94-6483-107-8

This research study was supported by a research grant of the Dutch National Institute for Public Health and the Environment (RIVM), the Netherlands, for local Public Health Services.
The work presented in this thesis was carried out within the Radboud Institute for Health Sciences.

Provided by thesis specialist Ridderprint, ridderprint.nl
Printing: Ridderprint
Layout and design: Sara Terwisscha van Scheltinga, persoonlijkproefschrift.nl
Cover design and layout images: Bert Mulder

Vaccine Decision-Making and Vaccine Acceptance among orthodox Protestants in the Netherlands

Proefschrift

ter verkrijging van de graad van doctor
aan de Radboud Universiteit Nijmegen
op gezag van de rector magnificus prof. dr. J.H.J.M. van Krieken,
volgens besluit van het college voor promoties
in het openbaar te verdedigen op

donderdag 8 juni 2023
om 10.30 uur precies

door

Anne Cecile Mulder
geboren op 28 maart 1987
te Ede

Promotoren

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Copromotoren

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Paranimfen

Merthe Broekman-Mulder

Rodin Aarssen

Voor mijn oma, Elisabeth Bennink-Oltvoort

en alle andere vrouwen die graag hadden willen gaan studeren,
maar daar niet de mogelijkheid toe kregen.

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Chapter 1

General introduction

Introduction

Vaccination is one of the most effective public health interventions against infectious diseases. Vaccine development and large-scale vaccination campaigns have prevented millions of deaths by infectious diseases worldwide.[1-3] Due to vaccines, smallpox has been eradicated, and poliomyelitis counts only a few wild poliovirus cases worldwide annually.[4] Before the introduction of the measles vaccine, nearly all children were infected with measles, a highly infectious disease with a mortality rate of 0.1% in high-income countries.[5] Between 2000-2018, measles vaccinations reduced the number of measles deaths with 73%, preventing more than 23 million deaths worldwide.[6] Nowadays, most cases of vaccine preventable diseases (VPDs) occur in low-income countries, as vaccination coverages in these countries are suboptimal due to poor access to immunization and health services. [7] In many countries getting vaccinated is voluntary, or exemptions are allowed based on philosophical or religious grounds.[8] Therefore, individuals can decide for themselves whether to accept vaccination or not. Low or decreasing vaccination rates are not only caused by lack of access, due to geographical and practical barriers, but also by intentional vaccine refusal.[9]

Vaccine hesitancy and vaccine refusal as a public health problem

Despite the enormous reduction in VPDs since the introduction of vaccines, not everyone is convinced of the positive effect of vaccinations. In 2019, 84% of the world population believed that vaccines are effective and 79% considered vaccines to be safe.[10] Confidence in vaccine safety is generally lower in high-income regions. In 2018, the perceived vaccine safety among people in Northern America was 72% and 73% in Northern Europe, compared to 95% in South Asia and 92% in Eastern Africa. The World Health Organization (WHO) identified vaccine hesitancy as one of the top ten threats to global health.[11] The Strategic Advisory Group of Experts on Immunization (SAGE) Working Group on Vaccine Hesitancy defined vaccine hesitancy as ‘the reluctance to receive vaccinations despite the availability of vaccines’.[9] Vaccine hesitancy is closely related to vaccine objection, as individuals may decide to refuse one or more vaccinations based on their vaccine concerns. Growing vaccine refusal leads to gaps in populations’ herd immunity, which can result in VPD outbreaks.[12] As a result, countries that were close to eliminating measles, saw a resurgence of this VPD caused by vaccine refusal.[13, 14]

The increase in vaccine hesitancy can be explained by several developments. Firstly, the success of vaccination programs has dramatically reduced the number of infectious diseases. As a result, individuals do not have first-hand knowledge of

the consequences of VPDs and the suffering these diseases cause, which reduces the visibility of the direct and indirect benefits of vaccination.[15] Secondly, The Internet and social media have become important sources for vaccination information, facilitating faster and cross-border access to anti-vaccination information and negative vaccine sentiments.[16, 17] Thirdly, vaccine hesitancy increases due to the rise of health care consumerism and patient empowerment in health decision-making.[18, 19] The modern 'informed' patient wants to actively participate in the decision-making process concerning their own health. Some individuals consider vaccine refusal as a healthy choice consistent with a consciously healthy lifestyle. From their perspective, accepting unnaturally produced vaccinations is something the uninformed, unhealthy mainstream does.[20, 21]

In their definition of vaccine hesitancy, the SAGE Working Group defines vaccine hesitant persons as individuals who refuse all or some vaccinations, delay vaccinations, or are unsure whether or not to vaccinate. This definition does not distinguish between individuals who have doubts about vaccinations and have not yet made a vaccination decision, and individuals who easily decide to refuse vaccination without having doubts. This distinction is of great importance as vaccine hesitancy and vaccine refusal require a different approach in vaccine policy and vaccination care. A review aimed to clarify the concept of vaccine hesitancy proposes that vaccine hesitancy should be defined as a psychological state of indecisiveness that people may experience when making a decision regarding vaccination.[22] The authors explicitly separate vaccine hesitancy from vaccination behaviour, e.g. accepting or refusing vaccinations.

Expanding vaccine target populations and vaccine decision-making

Traditionally, large-scale vaccination campaigns were primarily aimed at (young) children, with parents having to decide whether or not to accept vaccinations for their child. This practice shifted when vaccines became available for adult target groups (influenza, Hepatitis B, and pneumococcal vaccines), for pregnant women (influenza and pertussis vaccines), and for adolescents (human papillomavirus and meningococcal ACWY vaccines).[23] With the expansion of vaccination programmes for various age groups, adolescents and adults are confronted with multiple vaccine decision-making moments throughout their lives.[24] With the introduction of the maternal pertussis and maternal influenza vaccination, pregnant women have to make a vaccination decision for themselves and their unborn child. These vaccinations, administered to women during pregnancy, aimed to provide direct protection for the pregnant woman and passive immunity to her infant for several months after birth.[25]

Another new target group are adolescents and adults whose parents decided not to vaccinate them against measles and rubella as children. Adolescents and adults who were not infected during their childhood, may have to decide whether they want to catch-up these vaccinations later in their life, as both measles and rubella can cause severe complications at a later age and during pregnancy.[26]

Under-vaccinated groups and disease outbreaks

Vaccination decision-making is often viewed as an individual process, even though deciding not to accept a vaccination offer has consequences for the society when this refusal leads to spread of VPDs. Nonetheless, deciding to refuse vaccinations is also observed in group context. An under-vaccinated group can be defined as 'a group of persons who share the same beliefs and/or live in socially closeknit communities and who have or had historically low vaccination coverage and/or experienced outbreaks of VPDs'.[27] Well-known under-vaccinated groups are conservative religious groups -among which orthodox Jewish, orthodox Protestant, and Amish communities-, migrant populations -among which Roma, Sinti and Irish Travellers-, ethnic minorities, and anthroposophical societies.[27-29] Low vaccination uptake among under-vaccinated groups can be due to practical barriers, such as lower access to health care facilities and/or language difficulties.[29, 30] However, vaccination objections among under-vaccinated groups are often based on, or strengthened by, their shared religious, philosophical or natural beliefs that conflict with immunisation.[27]

Under-vaccinated groups may have group-specific vaccine objecting arguments, yet, certain similar basic principles appear across different subgroups. Many under-vaccinated groups express concerns about vaccine safety, vaccine efficacy, and overloading the immune system by combining different vaccines.[29, 31-35] Nevertheless, the belief that experiencing infectious diseases, and thereby allowing the body to produce its own antibodies, is essential for a child's development is found primarily among anthroposophical societies.[31, 32] Several under-vaccinated groups mention faith in natural and traditional remedies, and the belief that naturally developed immunity is superior to vaccination.[36, 37] Various religious under-vaccinated groups believe that accepting vaccination implicitly reflects doubt of divine intentions.[35, 38, 39] Some religious communities refuse a specific vaccination as the vaccine contains substances prohibited by their religious laws, such as nutritional products that violate dietary regulations or cells derived from an aborted fetus that violate their prolife views.[40] Regarding human papillomavirus (HPV)-vaccination, which prevents the sexually transmitted HPV-infection, several under-vaccinated groups expressed that this vaccination contradicts their beliefs concerning the moral values of no sex before marriage and partner for life.[34, 41, 42] For many under-

vaccinated groups, an additional argument for vaccine refusal is their distrust in the government and health institutions that provide the vaccination.[32, 43, 44]

Under-vaccinated groups are repeatedly involved in VPD outbreaks. Over the past decade, large measles outbreaks occurred in orthodox Jewish communities in London (2013), Jerusalem (20182019), and New York (2018-2019); in Amish communities in Ohio (2017); in the orthodox Protestant community in the Netherlands (2013-2014); in Roma communities in Greece (2017); and in an Somali community in Minnesota (2017).[45-50] Geographic clustering and strong social interaction in an under-vaccinated group increases transmission of a VPD among susceptible individuals . The extent of a VPD-outbreak depends on the number of susceptible individuals within the group, their level of interaction, and the group size.[51] When interaction outside the under-vaccinated group occurs, a VPD can also spread among unvaccinated individuals who are not part of this group or community. Consequently, a VPD outbreak can pose a health risk to individuals outside the group who are not vaccinated for personal reasons, but also because of their age or frail health.

Large-scale VPD outbreaks cause individual health damage to infected individuals, and impose a great burden on health care systems and governments.[52, 53] However, when a large majority of the unvaccinated population is protected by natural immunity, a new outbreak of the VPD is unlikely to occur in the near future.[51] The consequence, however, is that when a new VPD occurs in the under-vaccinated population after many years, susceptible individuals are infected at a later age, often accompanied by a higher risk of complications.[54]

Orthodox Protestants in the Netherlands

History of vaccine objection among orthodox Protestants

The Dutch orthodox Protestant community is historically well-known for their objections to vaccination. Important topics in the religious experience of the orthodox Protestant community are complete trust in the Word of God, God's sovereignty, and predestination.[55, 56] The orthodox Protestant church movement originated in the Reformation in the 16th century in Europe, based on the theological ideas of reformer John Calvin (1509-1564). Dutch orthodox Protestants highly value intense religious experiences and maintain strict adherence to the Bible and three confessionals scriptures: the Belgic Confession (1561), the Heidelberg Catechism (1563), and the Canons of Dordt (1619).

For these orthodox Protestants, engaging and maintaining a personal relationship with God is most important.[56] Therefore, they highly value justifying their decisions

to God, including decisions regarding acceptance or rejection of vaccinations. [35, 57] The Bible and the three confessional scriptures were written before the introduction of the first smallpox vaccination at the beginning of 19th century. However, interpretation of biblical texts and religious writings support believers to outline their opinion on vaccination.[58] A common argument against vaccination derives from Lord's Day 10 of the Heidelberg Catechism about God's Providence. Lord's Day 10 states that health and sickness do not come to mankind by chance, but by God's fatherly hand. Preventive measures to protect against possible future harm, including vaccination, should be rejected as men should not interfere with the divine providence.[58] Religious arguments mentioned by orthodox Protestants in favour of accepting vaccination are that vaccination is a gift from God which may be used in faith and gratitude, and that God has given knowledge to mankind which men should use wisely.[35, 59]

The religion-based vaccination resistance among Dutch orthodox Protestants started with the implementation of the smallpox vaccination campaigns in the 19th century.[60] The initial vaccination resistance was fuelled by published statements of an orthodox Protestant physician, Abraham Capadose, in 1823. Capadose's anti-vaccination plea was based on the concepts that the smallpox vaccine was an assault on a healthy body (as the vaccination could cause severe side-effects) and that disease prevention by vaccination interferes with divine providence.[61] The introduction of mandatory smallpox vaccination for teachers and children for school admission in 1872 further increased the orthodox Protestants' vaccination protest. [60] In 1928, orthodox Protestants negotiated an exception to vaccination obligation for conscientious objectors with the Dutch government.[62]

Nowadays, vaccine hesitancy and objection among the orthodox Protestants is often a blend of theological objections, the desire for freedom of personal decision-making based on their religious belief, supplemented by medical concerns.[58, 60, 63, 64] Frequently mentioned vaccination-objecting medical arguments among orthodox Protestants are the potential side-effects after vaccination, that natural infections provide higher and longer-lasting protective antibodies than vaccination, and the assumption that vaccination is unnecessary associated with their lifestyle (HPV-vaccination).[35, 63-65]

Present day orthodox Protestant community

Today, the orthodox Protestant community consists of an estimated 250.000 persons, which is approximately 1.5% of the Dutch population.[66-70] Roughly three-quarter of the orthodox Protestants live geographically in the so-called Dutch Bible belt, which stretches from the south-west to the north-east of the Netherlands.[69] In addition to

geographic allegiance, the community also has a strong socio-cultural commitment, founded on their shared religious beliefs.

The close-knit orthodox Protestant community has its own political party, schools, national newspaper, radio broadcast, magazines, social media channels, and local clubs and societies. The orthodox Protestant political party, the Reformed Political Party (SGP), has had a consistent number of voters among their orthodox Protestant constituencies since its founding in 1918, and generally has two or three seats in the House of Representatives.[71] Bible belt municipalities are often identified as municipalities with a high number of SGP-voters (Figure 1).[69, 72] The establishment of orthodox Protestant schools was made possible with the introduction of Dutch freedom of education in 1917. Currently, there are more than 160 orthodox Protestant elementary schools, seven orthodox Protestant high schools, one orthodox Protestants vocational school, and one orthodox Protestant university of applied science.[73] Most of these schools are located in or nearby Bible belt municipalities. Orthodox Protestants prefer to marry young and often have large families.[74] They are characterised by a carefully maintained appearance, with women and girls wearing skirts and dresses. Traditionally, orthodox Protestants refrain from sports, competitions, games and watching television, and especially avoid non-religious outgoing activities on Sunday. The Internet is used, however, often applied with special internet filtering.[75]

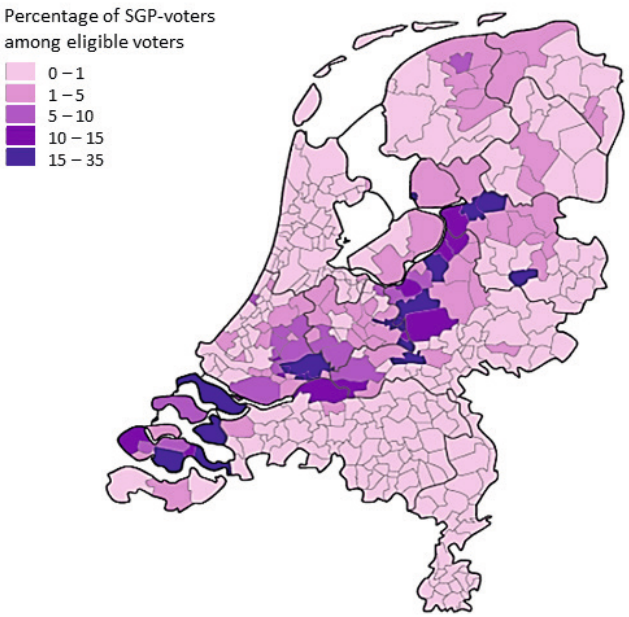

Figure 1. Municipal SGP-voting proportions the Dutch National Elections for seats in the House of Representatives 2021 [76, 77]

Although the orthodox Protestant community is often referred to as one united group, distinctions can be made between different denominations, which vary in their degree of conservatism.[56] The community has known many church secessions in the past and present, yet, five main church denominations can be outlined. The most conservative denominations are the Reformed Congregations in the Netherlands (Gereformeerde Gemeenten in Nederland) and Old Reformed Congregations (Oud Gereformeerde Gemeenten in Nederland). Moderately conservative denominations are the Restored Reformed Church (Hersteld Hervormde Kerk) and Reformed Congregations (Gereformeerde Gemeenten). Least conservative denominations are the pietistic branch 'Bewaar het Pand' within the Christian Reformed Churches (Christelijke Gereformeerde Kerken) and the Reformed Bond within the Protestant Church in the Netherlands (Gereformeerde Bond binnen de Protestantse Kerk in Nederland). The Reformed Bond is a small orthodox Protestant branch within the Protestant Church in the Netherlands.

Current vaccination coverage among orthodox Protestants

The orthodox Protestant community is generally known as a vaccine objecting community. Nevertheless, the majority of the orthodox Protestant parents accepts vaccinations for their children (60%).[78] A study in 2017 concluded that this vaccination coverage is gradually increasing over generations.[79] About 65% of young orthodox Protestant (prospective) parents accept, or plan to accept, vaccinations for their children. Nonetheless, in the most conservative denominations, childhood immunization uptake remains low, with an overall coverage of <25%. The vaccination coverage of moderately conservative church denominations varies between 50-75%, and the least conservative church denominations have the highest average vaccination coverage of more than 85%.[78, 79]

On a national scale, the Dutch Bible belt is clearly reflected on the map of municipal vaccination coverage (Figure 2). With low vaccination rates in these municipalities, the Bible belt is more susceptible to VPD outbreaks (Figure 3). The last large measles epidemic occurred in 2013-2014 (2700 reported cases nationally), 14 years after the measles epidemic of 1999-2000 (3292 reported cases nationally).[54, 80] The last rubella outbreak occurred in 2004-2005 (387 reported cases nationally).[81] The prolonged absence of rubella outbreaks increases the risk of contracting rubella during pregnancy (resulting in miscarriages and congenital malformations) among a growing number of unvaccinated orthodox Protestant women. Although the vaccination coverage among orthodox Protestants is slightly increasing, unvaccinated orthodox Protestant adolescents and adults who have not acquired natural immunity are at risk for infection during future VPD outbreaks.

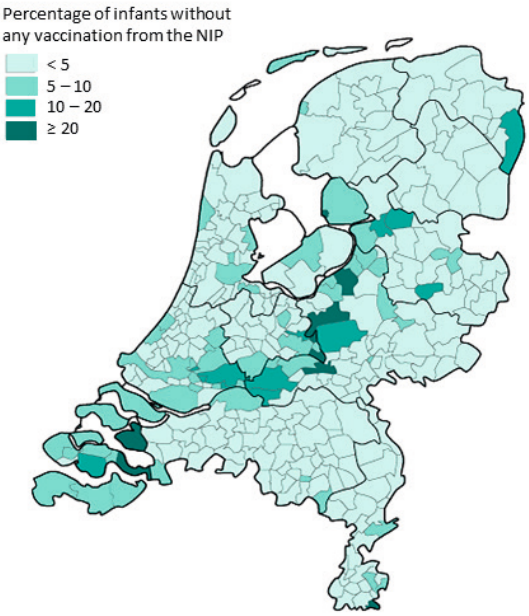

Figure 2. Percentage of infants who did not receive any vaccinations from the National Immunisation Programme [82, 83]

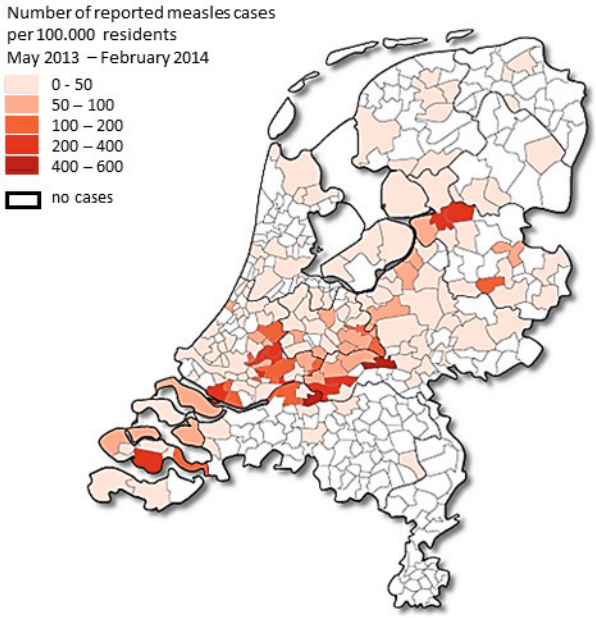

Figure 3. Incidence of measles cases May 2013 to February 2014 in the Netherlands [84]

Vaccine decision-making among orthodox Protestants

The study of Ruijs et al. (2012) on vaccine decision-making found that a proportion of the orthodox Protestant parents accept or refuse vaccination for their child based on family tradition, yet, other orthodox Protestant parents make a deliberate vaccination decision.[35] The study of Spaan et al. (2017) confirms that the decision to accept or refuse vaccinations for future children is not predetermined for all orthodox Protestant parents, as 20% of the study respondents without children had not yet made a decision about accepting or refusing vaccinations for their future children.[79]

Ruijs et al. (2012) showed that vaccination decisions are sometimes preceded by lengthy discussions between the two orthodox Protestant parents, in which religious arguments and personal faith in God are important topics.[35] Parents who decided not to vaccinate their child were aware of the medical risks involved; they feared that their children might become seriously ill or die during a VPD outbreak. Some parents who deliberately decided to vaccinate their child feared that God might not agree with their decision, and feared immediate punishment from God.[35] Unexpected medical events after vaccination, such as side-effects, were interpreted as a sign from God, resulting in the decision to stop vaccination.

A study among health care providers (HCPs) who worked in the Dutch Bible belt area showed that HCPs often primarily respond to vaccine objections among orthodox Protestants by providing medical information and correcting any misconceptions regarding vaccination.[85] Most HCPs found it difficult to adequately engage in the vaccine decision-making process of orthodox Protestant parents. Only HCPs who were member to the orthodox Protestant community themselves were actively consulted by orthodox Protestant parents who were hesitant about vaccination.

Aim and outline of this thesis

The main aim of this thesis is to gain insight into the vaccination decision-making process of orthodox Protestants and to obtain more in-depth understanding of factors related to vaccination acceptance concerning adolescent and adult vaccinations in this group.

This thesis starts with outlining the orthodox Protestant community in perspective to other under-vaccinated groups. In the Netherlands, the orthodox Protestants are traditionally viewed as the most prominent under-vaccinated group at risk of infectious disease outbreaks. The aim of **Chapter 2** is to examine HPV-vaccination acceptance among orthodox Protestants and other under-vaccinated groups by determining the influence of ethnicity, socioeconomic status, and political voting

behaviour on vaccination uptake in an ecological database study. HPV-vaccination uptake was chosen as outcome measure, as HPV-vaccination is characterized by its low uptake and fluctuation in uptake over time compared to other vaccinations in the National Immunisation Programme.

The second part of thesis focusses on the impact of being unvaccinated as a child on infectious disease risk later in life among orthodox Protestants. As a result of their parents' vaccination decision, unvaccinated adolescents and young adults may still be susceptible to VPDs such as measles and rubella and, therefore, eligible for catch-up vaccination to prevent measles or rubella infection in the future. **Chapter 3** aims to identify characteristics of unvaccinated orthodox Protestant adolescents and young adults associated with persisting measles susceptibility to determine risks factors for acquiring measles at a later age using a case-control design. **Chapter 4** presents a mixed-methods study conducted among unvaccinated women of childbearing age aimed to determine personal experience with rubella, perceived rubella susceptibility, and intention to accept rubella screening and vaccination to prevent rubella infection during pregnancy.

The third part of this thesis focusses on the vaccine decision-making process among orthodox Protestants. Although a fair amount is known about the vaccination coverage among the orthodox Protestant community, little is known about their decision-making process and what their needs are for making a vaccination decision. **Chapters 5** and **6** aim to provide insight into the decision-making process and intention towards maternal pertussis vaccination among orthodox Protestant women of childbearing age. In **chapter 5** the decision-making process and decision-making needs regarding maternal pertussis vaccination is explored, using in-depth interviews and online focus groups. In **chapter 6**, women's decision-making process is quantified in a survey study. The first objective in this study is to examine orthodox Protestant women's information needs, conversation needs, and needs concerning HCPs, including determining the association between women's decision-making needs and their intention to accept maternal pertussis vaccination. The second objective is to explore the association between women's values consideration in the deliberation stage and their intention to vaccinate.

Chapter 7 provides a general discussion of the main findings from the previous chapters and recommendations for health care providers, public health policy makers and future research aimed to optimise informed and deliberate decision-making among under-vaccinated subgroups, orthodox Protestants in particular.

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Chapter 2

Determinants of HPV-vaccination uptake and subgroups with a lower uptake in the Netherlands

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BMC Public Health, 2021;21:1848

Abstract

Background

In the Netherlands, the HPV-vaccination uptake was 52% during the 2009 catch-up campaign (birth cohorts 1993–1996). This increased to 61% in the regular immunization program (birth cohorts 2000– 2001). However for birth cohorts 2003–2004 the uptake declined to 45.5%. With this study we aimed to gain insight into social, economic and cultural determinants that are associated with HPV-vaccination uptake and which subgroups with a lower HPV-vaccination uptake can be identified. In addition, we investigated whether the influence of these factors changed over time.

Methods

To study the determinants of HPV-vaccine uptake we performed a database study using different aggregation levels, i.e. individual level, postal code level and municipality level. All Dutch girls who were invited for HPV-vaccination through the National Immunization Program in the years 2012, 2014 and 2017 (i.e. birth cohorts 1999, 2001 and 2004, respectively) were included in the study population. We conducted multilevel logistic regression analyses to analyse the influence of the determinants on HPV-vaccination uptake, taking into account that the delivery of HPV-vaccine was nested within municipalities.

Results

Results showed that in particular having not received a measles-mumps-rubella (MMR)-vaccination, having one or two parents born in Morocco or Turkey, living in an area with lower socioeconomic status and higher municipal voting proportions for Christian political parties or populist parties with liberal-conservative views were associated with a lower HPV-vaccination uptake. Besides some changes in political preferences of the population and changes in the association between HPV-vaccination uptake and urbanization level we found no clear determinants which could possibly explain the decrease in the HPV-vaccination uptake

Conclusions

In this study we identified current social, economic and cultural determinants that are associated with HPV-vaccination uptake and which low-vaccination subgroups can be identified. However, no clear determinants were found which could explain the decrease in the HPV-vaccination uptake. Tailored information and/or consultation for groups that are associated with a lower HPV-vaccination uptake might help to increase the HPV-vaccination uptake in the future.

Key words: Immunization, Human papillomavirus (HPV), Ethnicity, Urbanization, Socio-economic status, Political preference

Background

Vaccination against human papillomavirus (HPV) targeting girls 12 years of age is part of the Dutch National Immunization Program (NIP) since 2010. Prior to this, a catch-up campaign for 13–16-year old girls was initiated in 2009. The bivalent HPV16/18-vaccine was used starting with a three-dose schedule up to 2013 and a two-dose schedule from 2014 onwards. HPV16 and −18 together are estimated to account for 70% of all cases of cervical cancer.[1] In the Netherlands, annually about 800 women are diagnosed with cervical cancer and about 200 die due to this disease.[2, 3]

The HPV-vaccination uptake is low compared to the coverage for other vaccines in the Dutch NIP. During the catch-up campaign in 2009, the vaccine coverage was 52% for birth cohorts 1993–1996.[4] This increased to 61% for birth cohorts 2000 and 2001 but declined thereafter to 45.5% for birth cohorts 2003 and 2004.[5] In addition, large variations in the vaccination coverage were observed at municipality level ranging from less than 10% to more than 80%.[6]

Research among girls who were targeted for the initial catch-up campaign and their mothers showed that sociodemographic determinants, such as socioeconomic status (SES) and country of birth were associated with HPV-vaccination uptake.[7, 8] In addition, various Christian groups have objections to HPV-vaccination because it concerns protection against a sexually transmitted infection or because they have religious objections to vaccination in general.[7, 9, 10] Previous studies indicate that in several high income countries lack of trust in the government also plays a role in the willingness to get HPV-vaccination.[11-13] An ecological study conducted in the United States showed that political colour is associated with vaccination uptake in adolescence, as well.[14] In the Netherlands, high political preference for Protestant-Christian parties at municipality level was previously found to be associated with low HPV-vaccination uptake.[7] Political preference for other political parties might also be associated with low HPV-vaccination uptake, because of the relation with confidence in government institutions, media and social institutions.[15, 16]

It is unknown whether the influence of the various social, economic and cultural determinants on HPV-vaccination uptake changed over time in the Netherlands. In addition, it is unknown which determinants could explain the recent decrease in the HPV-vaccination uptake. With this study, we aim to gain insight into the determinants that are associated with HPV-vaccination uptake and which low-vaccination subgroups can be identified, and to investigate whether target groups can be identified that are associated with the decline in HPV-vaccination uptake.

Methods

Sample and data collection

We performed a database study to investigate various determinants of HPV-vaccination uptake on different aggregation levels: individual, postal code and municipality. The sample included all girls invited for HPV-vaccination through the NIP in the years 2012, 2014 and 2017, respectively from birth cohorts 1999, 2001 and 2004. For 2017 was the latest complete dataset available; in 2014 the vaccination schedule was changed and this was the last year before the decline in vaccination uptake; in 2012 and 2017 the Dutch National Elections for seats in the House of Representatives were held.

Anonymous individual-level data were obtained retrospectively in 2018 from the national vaccination register (Praeventis), using the 2018 municipality division (380 municipalities). The individual level variable Ethnicity was defined as country of birth of both parents, for which most common country of birth combinations were used.

Additional data, on postal code and municipality level, were extracted from the publicly available data of Statistics Netherlands (CBS), The Netherlands Institute for Social Research (SCP), and the Electoral Council (Kiesraad), or were provided by the Municipal Health Services (MHS). If data was not available for a certain invitation year, data of the most recent year was used (see Table 1 for variable details).

The postal code level variable Socioeconomic status was defined as status score, which is calculated by the SCP based on the educational level, paid jobs and income of households. Road distance was defined as distance by car between girls' home address and vaccination location in kilometres.

Voting proportions from the National Elections for political parties with 2 or more seats in the House of Representatives were included in the analyses. Supplementary material 1 contains a list of these political parties and the distribution of seats in the House of Representatives in the Dutch National elections of 2012 and 2017.[17]

Table 1. Characteristics of variables: level of aggregation, measurement level, year of data collection for each invitation year and original database

Variable	Measurement level	Invitation Year [1]	Year of data collection [2]	Database
Individual-level				
HPV-vaccination status (dependent variable)	Dichotomous: Completed series of HPV-vaccinations; 0=has no completed HPV-vaccination series; 1=has a completed HPV-vaccination series (2012: 3-doses; 2014/2017: 2-doses)	2012 2014 2017	2018 2018 2018	Praeventis
MMR-vaccination status	Categorical: Zero, one, two doses of MMR-vaccination	2012 2014 2017	2018 2018 2018	Praeventis
DT(aP)-IPV-vaccination status	Categorical: Zero, primary series (3-doses), completed series (6-doses) of DT(aP)-IPV-vaccination	2012 2014 2017	2018 2018 2018	Praeventis
Ethnicity [3]	Categorical: 14 combinations of parents' country of birth and the category unknown (one or both parents' country of birth is unknown) [4]	2012 2014 2017	2018 2018 2018	Praeventis
Postal code-level				
Socioeconomic status (SES)	Categorical: Status score low (≤-1.0000), low-intermediate (-0.9999 to 0.0000), high-intermediate (0.0001-0.9999), high (≥1.0000)	2012 2014 2017	2010 2014 2016	SCP
Road distance	Categorical: 0 km (HPV-vaccination provided in same postal code as home address), 0-5 (0.1-4.9) km, 5-10 (5.0-9.9) km, ≥10 km	2014 2017	2014 2017	MHS
Municipality-level				
Urbanization level [5]	Categorical: Very high (>2500 addresses per km2), High (1500-2500 add. per km2), Moderately high (1000-1500 add. per km2), Low (500-1000 add. per km2), Very low (<500 add. per km2)	2012 2014 2017	2017 2017 2017	CBS
Voting proportions from the National Elections for political parties [6]	Dichotomous: Voting proportion (percentage of votes per political party) lower or higher than the mean of the national voting proportion of the party.	2012 2014 2017	2012 2012 2017	Electoral Council

Abbreviations: HPV= Human Papillomavirus; MMR= Mumps-measles-rubella; DTaP-IPV= diphtheria-tetanus-pertussis-polio; SCP= The Netherlands Institute for Social Research; MHS= Municipal Health Services; CBS= Statistics Netherlands; km=kilometre. Praeventis= National vaccination registry.

[1] Girls invited for HPV-vaccination through the NIP in the years 2012, 2014 and 2017 were born in

1999, 2001 and 2004 respectively.

[2] If data was not available for a certain invitation year, data of the most recent year was used.

[3] From December 2002 onwards, parents' country of birth was authorized from the Personal Records Database (Dutch: BRP, previously known as GBA) and therefore more complete for girls invited in 2017 (birth cohort 2004) than for girls invited in 2012 and 2014 (birth cohorts 1999 and 2001).

[4] The Netherlands-The Netherlands, The Netherlands-Turkey, Turkey-Turkey, The Netherlands-Morocco, Morocco-Morocco, The Netherlands-Surinam, Surinam-Surinam, The Netherlands-Netherlands Antilles and Aruba, Netherlands Antilles and Aruba-Netherlands Antilles and Aruba, The Netherlands-other western country, other western country-other western country, The Netherlands-other non-western country, other non-western country -other non-western country, other western country-other non-western country, unknown.

[5] In the database the urbanization level of 2017 was used; the most recent HPV-vaccination invitation year. Following the municipal re-division between 2017 and 2018, several municipalities merged into three new municipalities. For these three new municipalities we used the urbanization level of 2018.

[6] Ten variables: 1) People's Party for Freedom and Democracy (VVD; right-wing liberal party with more progressive positions in ethical matters), 2) Labour Party (PvdA; progressive, social-democratic party) & Denk (DENK; movement for migrants and a "tolerant and solidary society"; political party founded in 2015 by former members of the PvdA), 3) Party for Freedom (PVV; populist party with both conservative, liberal "right" and "left" views) & Forum for Democracy (FvD; conservative, right-wing populist Eurosceptic political party; political party founded in 2015, whose voters are mainly former PVV voters), 4) Socialist Party (SP; socialist, Eurosceptic party which has a strong local, action-oriented basis), 5) Christian Democratic Appeal (CDA; Christian-inspired party at the center of the political spectrum), 6) Democrats 66 (D66; reformist social-liberal party), 7) Christian Union (CU; Christian party, with progressive positions in the social and ecological field and conservative positions on ethical issues) & Reformed Political Party (SGP; conservative Christian (Reformed) party that wants to conduct politics strictly according to Biblical standards), 8) Green Left (GL; progressive party which attaches great importance to sustainability), 9) Party for the Animals (PvdD; testimonial party with main goals animal rights and animal welfare), 10) 50PLUS (50+; party that stands up especially for the interests of people aged 50 and over). The voting proportions for the three new municipalities in 2018 were calculated based on the weighted averages of the voting proportions of the previous municipalities before they were merged into the new municipality.

Statistical analysis

Multilevel logistic regression analyses were used to determine the association between the dependent variable HPV-vaccination uptake of a completed series (2 or 3 doses depending on invitation year) and predictor variables. The multilevel models included two hierarchical levels where girls who were invited for HPV-vaccinations (level 1) were nested in municipalities (level 2). First, the associations between HPV-vaccination uptake and independent variables (Table 1) were measured using multilevel univariate logistic regression analyses.[18] Road distance to the vaccination location, SES and voting proportions for political parties were included on a categorical scale -instead of interval scale- to assess the relative effect of the predictor variables.[19] Secondly, multilevel multivariable logistic regression analysis was conducted. Predictor variables were selected based on a statistically significant association with HPV-vaccination uptake following the multilevel univariate logistic regression analysis ($p < 0.05$) unless multicollinearity (> 0.70) was found between two or more predictor variables. To calculate the correlation between all predictor variables in order to detect multicollinearity Spearman's correlation coefficient and the phi coefficient (2 × 2) were used.[18] In the multilevel multivariable logistic

regression analysis, we used two different main models (Fig. 1). Model 1 contained a separate multilevel multivariable logistic regression model for each of the invitation years (2012, 2014 and 2017). In model 2, we combined the data of three invitation years using an additional variable for invitation year (categorial) and an interaction variable invitation year*predictor variable, to measure the effect of change of the predictor variables over time.

All analyses were performed using IBM SPSS Statistics®, version 24. Associations between HPV-vaccination uptake and predictor variables are shown with crude odds ratios (COR), adjusted odds ratios (AOR) and 95% confidence intervals (95%CI).

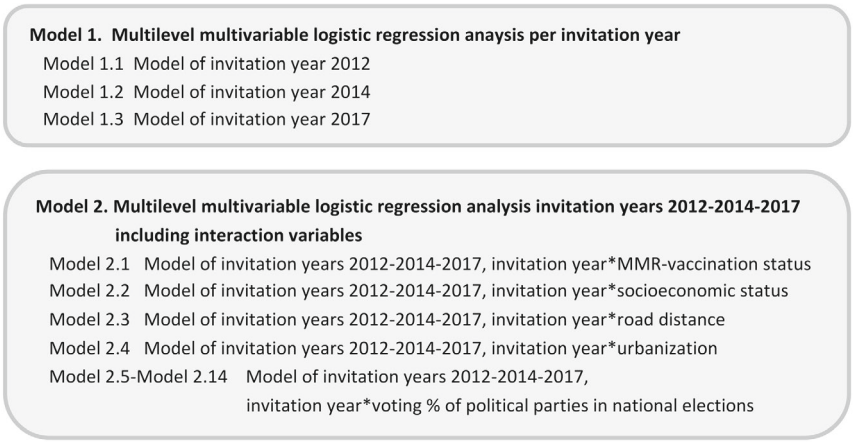

Figure 1. Multilevel multivariable models used for statistical analysis

Ethical considerations

The study was approved by the research ethics committee of the Radboud University Nijmegen Medical Centre, Nijmegen, the Netherlands; CMO number 2018/4744.

Results

In the following paragraphs, main results of the multilevel univariate and multivariable logistic analysis of the invitation year 2017 are presented per predictor variable. Additionally, these results are compared to the associations between HPV-vaccination uptake and the predictor variables in the invitation years 2012 and 2014. Tables of the multilevel univariate analysis (Table 2) and multilevel multivariable logistic regression model (Table 3; model 1.3 for girls invited for HPV-vaccination in 2017) are included in this article. Model 1.1. and 1.2. (for the girls invited in 2012 and 2014) and the models including the interaction variable between invitation years and each predictor variable (models 2.1–2.14) can be found in supplementary material 2.

Table 2. Descriptive analysis HPV-vaccination uptake and predictor variables on individual, postal code and municipality level (n = 299,883)

	2012				2014				2017			
Variable	**N**	**HPV-uptake %** [a]	**Multilevel univariate COR**	**p-value**	**N**	**HPV-uptake %** [a]	**Multilevel univariate COR**	**p-value**	**N**	**HPV-uptake %** [a]	**Multilevel univariate COR**	**p-value**
Total	102456	60.0%			100988	62.8%			96439	46.6%		
Individual level												
MMR-vaccination status	2012			<0.001	2014			<0.001	2017			<0.001
Zero vaccinations	5355	3.7%	reference	ref.	3190	6.6%	ref.	ref.	2548	6.0%	ref.	ref.
One vaccination	3079	28.4%	9.72	<0.001	3304	26.2%	4.68	<0.001	3162	13.3%	2.24	<0.001
Two Vaccinations	94022	64.3%	44.05	<0.001	94494	66.0%	25.34	<0.001	90729	48.9%	13.95	<0.001
DT(aP)-IPV-vaccination status	2012			<0.001	2014			<0.001	2017			<0.001
Zero vaccinations	5549	6.1%	ref.	ref.	3258	10.3%	ref.	ref.	2656	8.2%	ref.	ref.
Primary series	2851	28.2%	5.67	<0.001	3088	25.9%	2.81	<0.001	3539	20.0%	2.63	<0.001
Completed series	94056	64.2%	25.84	<0.001	94642	65.8%	15.50	<0.001	90244	48.7%	9.94	<0.001
Ethnicity	2012			<0.001	2014			<0.001	2017			<0.001
NLD - NLD	17319	63.6%	ref.	ref.	17761	65.2%	ref.	ref.	70614	49.4%	ref.	ref.
NLD - Turkey	352	32.4%	0.30	<0.001	405	34.6%	0.30	<0.001	1023	26.0%	0.34	<0.001
Turkey - Turkey	1306	27.9%	0.26	<0.001	1133	30.3%	0.25	<0.001	1802	20.5%	0.24	<0.001
NLD - Morocco	199	36.2%	0.36	<0.001	224	35.7%	0.34	<0.001	762	18.8%	0.22	<0.001
Morocco - Morocco	1272	18.2%	0.16	<0.001	1249	23.9%	0.20	<0.001	2920	16.5%	0.18	<0.001
NLD - Surinam	369	52.8%	0.73	0.003	414	54.8%	0.70	0.001	927	41.3%	0.71	<0.001
Surinam - Surinam	544	48.5%	0.68	<0.001	463	57.9%	0.86	0.108	708	45.6%	0.86	0.048
NLD - Ned Antilles/Aruba	186	51.6%	0.65	0.004	161	57.8%	0.74	0.058	475	35.6%	0.55	<0.001

Table 2. Descriptive analysis HPV-vaccination uptake and predictor variables on individual, postal code and municipality level (n = 299,883) (continued)

	2012				2014				2017			
Variable	**N**	**HPV-uptake % [a]**	**Multilevel univariate COR**	**p-value**	**N**	**HPV-uptake % [a]**	**Multilevel univariate COR**	**p-value**	**N**	**HPV-uptake % [a]**	**Multilevel univariate COR**	**p-value**
Ned Antilles/Aruba – Ned Antilles/Aruba	214	23.8%	0.20	<0.001	150	44.7%	0.45	<0.001	183	35.5%	0.57	<0.001
NLD - other WC	748	58.6%	0.84	0.020	858	64.1%	0.95	0.493	2331	51.0%	1.03	0.573
other WC - other WC	430	43.5%	0.44	<0.001	468	53.2%	0.62	<0.001	704	46.9%	0.84	0.025
NLD - other NWC	490	58.0%	0.84	0.071	581	59.9%	0.82	0.027	1673	50.0%	0.99	0.778
other NWC - other NWC	1184	47.6%	0.57	<0.001	1192	59.3%	0.83	0.004	2190	51.1%	1.05	0.252
other WC - other NWC	92	43.5%	0.50	0.001	104	44.2%	0.45	<0.001	196	35.7%	0.53	<0.001
Unknown	77751	61.2%	0.85	<0.001	75825	63.9%	0.94	0.003	9931	42.9%	0.74	<0.001
Postal code level												
Socioeconomic status [b]	2012			<0.001	2014			<0.001	2017*			<0.001
Low	17723	51.4%	ref.	ref.	19395	54.9%	ref.	ref.	18149	36.9%	ref.	ref.
Low-intermediate	29714	58.8%	1.27	<0.001	26556	62.9%	1.34	<0.001	25467	44.6%	1.36	<0.001
High-intermediate	38297	62.7%	1.50	<0.001	37747	64.4%	1.57	<0.001	34292	48.8%	1.64	<0.001
High	15981	65.3%	1.84	<0.001	16732	68.4%	1.93	<0.001	18099	54.8%	2.09	<0.001
Road distance	2012*			0.129	2014			0.031	2017			0.340
0 km	12694	60.3%	ref.	ref.	13661	62.3%	ref.	ref.	13104	45.8%	ref.	ref.
0-5 km	44246	59.3%	1.03	0.279	41395	62.0%	1.04	0.105	38045	46.9%	1.02	0.547
5-10 km	28986	60.6%	1.06	0.026	28560	63.9%	1.07	0.003	29079	46.7%	1.04	0.081
>10 km	16495	60.8%	1.05	0.115	17343	63.3%	1.05	0.072	16185	46.2%	1.02	0.333

Table 2. Descriptive analysis HPV-vaccination uptake and predictor variables on individual, postal code and municipality level (n = 299,883) (continued)

	2012				2014				2017			
Variable	**N**	**HPV-uptake % [a]**	**Multilevel univariate COR**	**p-value**	**N**	**HPV-uptake % [a]**	**Multilevel univariate COR**	**p-value**	**N**	**HPV-uptake % [a]**	**Multilevel univariate COR**	**p-value**
Municipality level												
Urbanization level [c]	2012*			0.020	2014*			0.134	2017			0.058
Very high	23398	53.3%	ref.	ref.	19446	57.9%	ref.	ref.	19280	45.3%	ref.	ref.
High	31870	60.3%	1.14	0.272	30512	62.9%	1.03	0.793	29502	46.1%	0.95	0.642
Moderately high	17260	62.7%	1.28	0.038	18314	64.0%	1.16	0.232	17512	47.9%	1.03	0.819
Low	21315	63.8%	1.36	0.007	23200	65.5%	1.22	0.099	21526	48.3%	1.07	0.572
Very low	8604	63.1%	1.25	0.062	9513	64.1%	1.11	0.390	8618	44.3%	0.87	0.266
Voting % political parties [d]	**2012**				**2014***				**2017**			
Lower or higher than national mean												
People's Party for Freedom and Democracy (VVD)												
Lower	64595	57.3%	ref.	ref.	60833	60.5%	ref.	ref.	58855	43.6%	ref.	ref.
Higher	37852	64.8%	1.30	<0.001	40152	66.3%	1.27	<0.001	37583	51.3%	1.47	<0.001
Labor Party (PvdA), Denk (DENK)												
Lower	36543	60.9%	reference	ref.	39038	62.7%	ref.	ref.	34880	46.7%	ref.	ref.
Higher	65904	59.6%	1.09	0.096	61947	62.9%	1.10	0.076	61558	46.5%	1.00	0.931
Party for Freedom (PPV), Forum for Democracy (FvD)												
Lower	57814	59.7%	reference	ref.	56784	62.3%	ref.	ref.	52307	48.1%	ref.	ref.
Higher	44633	60.5%	1.14	0.007	44201	63.5%	1.10	0.077	44131	44.8%	0.88	0.006

Table 2. Descriptive analysis HPV-vaccination uptake and predictor variables on individual, postal code and municipality level (n = 299,883) (continued)

	2012				2014				2017			
Variable	**N**	**HPV-uptake % [(a)]**	**Multilevel univariate COR**	**p-value**	**N**	**HPV-uptake % [(a)]**	**Multilevel univariate COR**	**p-value**	**N**	**HPV-uptake % [(a)]**	**Multilevel univariate COR**	**p-value**
Socialist Party (SP)												
Lower	52335	57.6%	reference	ref.	53199	59.8%	ref.	ref.	4665	44.3%	ref.	ref.
Higher	50112	62.6%	1.40	<0.001	47786	66.2%	1.45	<0.001	41773	49.5%	1.29	<0.001
Christian Democratic Appeal (CDA)												
Lower	77344	59.9%	ref.	ref.	73747	63.0%	ref.	ref.	71075	46.8%	ref.	ref.
Higher	25103	60.6%	0.94	0.201	27238	62.4%	0.97	0.487	25363	45.9%	0.94	0.221
Democrats 66 (D66)												
Lower	43514	59.9%	ref.	ref.	45849	61.2%	ref.	ref.	38093	42.7%	ref.	ref.
Higher	58933	60.1%	1.25	<0.001	55136	64.2%	1.30	<0.001	58345	49.1%	1.46	<0.001
Christian Union (CU), Reformed Political Party (SGP)												
Lower	78482	61.8%	ref.	ref.	75461	64.9%	ref.	ref.	71521	48.5%	ref.	ref.
Higher	23965	54.3%	0.59	<0.001	25524	56.7%	0.60	<0.001	24917	41.1%	0.62	<0.001
Green Left (GL)												
Lower	44692	62.0%	ref.	ref.	47846	63.2%	ref.	ref.	38670	45.0%	ref.	ref.
Higher	57755	58.6%	1.07	0.196	53139	62.5%	1.11	0.046	57768	47.6%	1.21	<0.001
Party for the Animals (PvdD)												
Lower	37964	61.9%	ref.	ref.	40832	63.7%	ref.	ref.	38633	46.7%	ref.	ref.
Higher	64483	59.0%	1.03	0.561	60153	62.2%	1.02	0.737	57805	46.5%	1.03	0.588

Table 2. Descriptive analysis HPV-vaccination uptake and predictor variables on individual, postal code and municipality level (n = 299,883) (continued)

	2012				2014				2017			
Variable	**N**	**HPV-uptake % [(a)]**	**Multilevel univariate COR**	**p-value**	**N**	**HPV-uptake % [(a)]**	**Multilevel univariate COR**	**p-value**	**N**	**HPV-uptake % [(a)]**	**Multilevel univariate COR**	**p-value**
50PLUS (50+)												
Lower	57554	58.1%	reference	ref.	55729	61.0%	ref.	ref.	55484	46.5%	ref.	ref.
Higher	44893	62.6%	1.31	<0.001	45256	65.0%	1.25	<0.001	40954	46.7%	1.10	0.052

Abbreviations: COR= crude odds ratio, MMR=mumps-measles-rubella, DT(aP)-IPV=diphtheria-tetanus-pertussis-polio, NL=the Netherlands, Ned Antilles/ Aruba= the Netherlands Antilles and Aruba, WC=western countries, NWC=non-western countries. km=kilometer, VVD=People's Party for Freedom and Democracy, PvdA=Labor Party, PVV=Party for Freedom, FvD=Forum for Democracy, SP=Socialist Party, CDA=Christian Democratic Appeal, D66=Democrats 66, CU=Christian Union, SGP=Reformed Political Party, GL=Green Left, PvdD=The Party for the Animals, 50+=50PLUS. For explanatory notes on the political parties we refer to Supplementary material 1.

(a) HPV-uptake %= % of total of girls (N) with a completed HPV-vaccination series. Girls invited in 2012 were offered a three-dose series, girls invited in 2014 and 2017 a 2-dose series.

(b) Socioeconomic status classification; low (≤-1.0000), low-intermediate (-0.9999 to 0.0000), high-intermediate (0.0001-0.9999), high (≥1.0000).

(c) Urbanization classification; Very high: >2500 addresses per km2, high: 1500-2500 addresses per km2, moderately high: 1000-1500 addresses per km2, low: 500-1000 addresses per km2, very low <500 addresses per km2.

(d) Voting % classification: higher or lower compared to the national mean.

* For this variable/ invitation year, data from the most recent year available was used (See Table 1 for variable details).

Table 3. Multilevel multivariable logistic regression analysis of invitation year 2017, model 1.3, (n=96,007; 99.6% of the girls included in model)

Variable	N	HPV-uptake % [a]	Adjusted OR (AOR)	95% CI	p-value
MMR-vaccination status					<0.001
Zero vaccinations	2541	6.0%	reference	ref.	ref.
One vaccination	3155	13.3%	2.38	1.96-2.89	<0.001
Two Vaccinations	90311	48.9%	14.69	12.44-17.35	<0.001
Ethnicity					<0.001
NL - NL	70228	49.4%	ref.	ref.	ref.
NL - Turkey	1021	26.1%	0.37	0.32-0.42	<0.001
Turkey - Turkey	1800	20.5%	0.27	0.24-0.31	<0.001
NL - Morocco	760	18.7%	0.23	0.19-0.28	<0.001
Morocco - Morocco	2920	16.5%	0.20	0.18-0.23	<0.001
NL- Surinam	924	41.5%	0.75	0.65-0.86	<0.001
Surinam - Surinam	707	45.7%	0.94	0.81-1.10	0.451
NL - Ned Antilles/Aruba	475	35.6%	0.60	0.49-0.73	<0.001
Ned Antilles/Aruba - Ned Antilles/Aruba	182	35.7%	0.83	0.60-1.15	0.266
NL - other WC	2320	51.0%	1.07	0.98-1.16	0.142
other WC - other WC	704	46.9%	1.17	0.99-1.37	0.065
NL - other NWC	1667	50.0%	1.03	0.93-1.14	0.555
other NWC - other NWC	2188	51.1%	1.25	1.14-1.37	<0.001
other WC - other NWC	196	35.7%	0.65	0.48-0.88	0.005
Unknown	9915	42.9%	0.91	0.87-0.95	<0.001
Socioeconomic status [b]					<0.001
Low	18149	36.9%	ref.	ref.	ref.
Low - intermediate	25467	44.6%	1.21	1.15-1.27	<0.001
High - intermediate	34292	48.8%	1.40	1.34-1.47	<0.001
High	18099	54.8%	1.68	1.59-1.77	<0.001
Road distance					<0.001
0 km	13104	45.8%	ref.	ref.	ref.
0-5 km	37943	46.9%	0.99	0.94-1.03	0.555
5-10 km	28925	46.7%	0.93	0.89-0.98	0.006
>10 km	16035	46.2%	0.90	0.85-0.95	<0.001
Urbanization level [c]					0.002
Very high	19258	45.3%	ref.	ref.	ref.
High	29441	46.1%	0.84	0.70-0.995	0.043
Moderately high	17432	47.9%	0.75	0.62-0.90	0.002
Low	21360	48.3%	0.89	0.74-1.08	0.244
Very low	8616	44.1%	0.86	0.70-1.05	0.131

Table 3. Multilevel multivariable logistic regression analysis of invitation year 2017, model 1.3, (n=96,007; 99.6% of the girls included in model) (continued)

Variable	N	HPV-uptake % [a]	Adjusted OR (AOR)	95% CI	p-value
Voting % People's Party for Freedom and Democracy (VVD) [d]					
Lower	58531	43.5%	ref.	ref.	ref.
Higher	37476	51.3%	1.22	1.12-1.33	<0.001
Voting % Labour Party (PvdA), Denk (DENK) [d]					
Lower	34742	46.8%	ref.	ref.	ref.
Higher	61265	46.5%	0.94	0.86-1.04	0.209
Voting % Party for Freedom (PVV), Forum for Democracy (FvD) [d]					
Lower	52033	48.1%	ref.	ref.	ref.
Higher	43974	44.8%	0.90	0.81-0.99	0.029
Voting % Socialist Party (SP) [d]					
Lower	54491	44.3%	ref.	ref.	ref.
Higher	41516	49.5%	1.39	1.27-1.53	<0.001
Voting % Christian Democratic Appeal (CDA) [d]					
Lower	70868	46.8%	ref.	ref.	ref.
Higher	25139	45.9%	0.89	0.80-0.99	0.026
Voting % Democrats 66 (D66) [d]					
Lower	37814	42.6%	ref.	ref.	ref.
Higher	58193	49.1%	1.17	1.05-1.30	0.003
Voting % Christian Union (CU), Reformed Political Party (SGP) [d]					
Lower	71226	48.5%	ref.	ref.	ref.
Higher	24781	41.1%	0.81	0.73-0.91	<0.001
Voting % Green Left (GL) [d]					
Lower	38470	45.0%	ref.	ref.	ref.
Higher	57537	47.6%	1.15	1.03-1.30	0.015
Voting % Party for the Animals (PvdD) [d]					
Lower	38403	46.7%	ref.	ref.	ref.
Higher	57604	46.5%	0.82	0.74-0.91	<0.001
Voting % 50PLUS (50+) [d]					
Lower	55213	46.5%	ref.	ref.	ref.
Higher	40794	46.6%	0.99	0.90-1.09	0.814

Abbreviations: OR=odds ratio, CI=confidence interval, MMR=mumps-measles-rubella, NL=the Netherlands, Ned Antilles/Aruba= the Netherlands Antilles and Aruba, WC=western countries, NWC=non-western countries, km=kilometre, VVD=People's Party for Freedom and Democracy, PvdA=Labour Party, PVV=Party for Freedom, FvD=Forum for Democracy, SP=Socialist Party, CDA=Christian Democratic Appeal, D66=Democrats 66, CU=Christian Union, SGP=Reformed Political Party, GL=Green Left, PvdD=The Party for the Animals, 50+=50PLUS. For explanatory notes on the political parties we refer to Supplementary material 1.

[a] HPV-uptake %= % of total of girls (N) with a completed HPV-vaccination series (2 doses).

[b] Socioeconomic status classification; low (≤-1.0000), low-intermediate (-0.9999 to 0.0000), highintermediate (0.0001-0.9999), high (≥1.0000).

[c] Urbanization classification; Very high: >2500 addresses per km2, high: 1500-2500 addresses per km2, moderately high: 1000-1500 addresses per km2, low: 500-100 addresses per km2, very low <500 addresses per km2

[d] Voting % classification: higher or lower compared to the national mean.

MMR- and DT(aP)-IPV-vaccination status

As the correlation between MMR-vaccination status and DT(aP)-IPV-vaccination status was >0.80 in the multicollinearity analysis, only MMR-vaccination status was included in the multilevel multivariable logistic regression models. In the multilevel univariate and multivariable models MMR-vaccinations status was significant and positively associated with HPV-vaccination uptake (Tables 2, 3 and supplementary material 2 – model 1.1, 1.2), indicating that girls who did not have a completed series of MMR-vaccination had a lower HPV-vaccination uptake.

Ethnicity

Overall, girls with one or two parents born in another country than the Netherlands (both western and non-western countries) had a significantly lower HPV-vaccination uptake compared to girls whose parents both were born in the Netherlands (Tables 2, 3 and supplementary material 2 – model 1.1, 1.2).

In each invitation year girls with one or two parents born in Morocco or Turkey showed a significantly lower HPV-vaccination uptake compared to girls with two parents born in the Netherlands (Table 3 and supplementary material 2 - model 1.1, 1.2).

Considering the high number of girls of whom the country of birth of one or two parents is unknown in 2012 and 2014, compared to less unknown values in 2017, the effect of change over time on ethnicity could not be compared in a multilevel multivariate logistic regression model.

Socioeconomic status (SES)

Girls who lived in lower SES postal code areas had a statistically significant lower HPV-vaccination uptake than girls who lived in higher SES postal code areas (Tables 2, 3, and supplementary material 2 - model 1.1, 1.2). In each invitation year the odds of having received a completed series of HPV-vaccination was highest among girls who lived in a high SES postal code area compared to girls who lived in a low SES postal code area, followed by girls who lived in a high-intermediate SES postal code area, and subsequently, girls who lived in a low intermediate SES postal code area (Tables 2, 3 and supplementary material 2 - model 1.1, 1.2).

Road distance

In 2017, the multilevel univariate logistic regression model indicated no statistical significant difference in HPV-vaccination uptake among girls who lived closer or further away from the vaccination location (Table 2). However, the multivariable models showed that girls who lived in a postal code area which was five or more kilometres from the postal code area of the vaccination location, had a very small but statistically significant lower odds of having received a completed series of HPV-vaccinations compared to girls living in the same postal code area as the vaccination location (Table 3 and supplementary material 2 - model 2.3). This association was not significant in the multilevel multivariable models of 2012 and 2014 (supplementary material 2 – model 1.1, 1.2).

Urbanization level

In the multilevel univariate logistic regression model no statistically significant association was found between municipal urbanization level and girls' HPV-vaccination uptake in 2017 (Table 2). In the multivariable logistic regression analysis (Table 3), girls who were invited for HPV-vaccination in 2017 and lived in a municipality with a high or moderately high urbanization level had a statistically significant lower HPV-vaccination uptake compared to girls who lived in a very high urban municipality. The multilevel multivariable logistic regression models of invitation year 2012 and 2014 showed that girls living in low and very low urban municipalities had a statistically significant higher HPV-vaccination uptake than girls living in very high urban municipalities (supplementary material 2 - model 1.1, 1.2). In the multilevel multivariable logistic regression analysis including the interaction variable invitation year*urbanization level, no statistically significant different effect was found for urbanization level between the invitation years 2012 and 2014. However, in invitation year 2017, the effect of urbanization is statistically significant different from invitation year 2012, i.e. the difference in HPV-vaccination uptake between different levels of urbanization becomes smaller (supplementary material 2– model 2.4).

Voting proportions of political parties in national elections

The multilevel univariate and multivariable logistic regression analysis of 2017 showed a positive association between HPV-vaccination uptake and municipal voting proportion for People's Party for Freedom and Democracy (VVD), Socialist Party (SP), Democrats 66 (D66) and Green Left (GL) (Tables 2 and 3). This indicates that girls who lived in a municipality with a higher voting proportion for these parties, compared to the national mean, had a statistically significant higher HPV-vaccination uptake. A negative association was showed between HPV-vaccination uptake and a municipal voting proportion for Party for Freedom and Forum for Democracy (PVV & FvD), Christian Democratic Appeal (CDA) -only in the multivariable model-, Christian

Union and Reformed political party (CU & SGP) and Party for the Animals (PvdD) -only in the multivariable model- (Tables 2 and 3). This indicates that girls who lived in a municipality with a higher voting proportion for these parties, compared to the national mean, had a lower HPV-vaccination uptake.

Girls who lived in a municipality with a higher voting proportion for the populist parties with liberal conservative views PVV & FvD had a significantly lower HPV-vaccination uptake in 2017, yet, in invitation years 2012 and 2014 either a positive or no statistically significant association between HPV-vaccination uptake and PVV & FvD voting proportion was found (Table 3 and supplementary material 2 – model 1.1, 1.2, 2.7). A strong negative association between the HPV-vaccination uptake and the municipal voting proportions for the conservative Christian parties CU & SGP was found for invitation years 2012, 2014 and 2017 (Table 2, Table 3, supplementary material 2 – model 1.2, 2.1,). This effect does not change over the invitation years (model 2.11).

Discussion

This study was performed to gain insight into the current relationship between social, economic and cultural determinants and the HPV-vaccination uptake of Dutch adolescent girls and whether the influence of these factors changed over time. Results showed that previous willingness to vaccinate (defined as MMR vaccination status), ethnicity, socioeconomic status of the postal code area, urbanization level of the municipality, road distance to vaccination location and municipal voting proportions in national elections were predictors for the HPV-vaccination uptake. Subgroups with a lower HPV-vaccination uptake in 2017 were in particular girls who have not received a MMR-vaccination (HPV-vaccine uptake 6.0% versus 48.9% when having received two MMR-vaccinations), who have one or two parents born in Morocco or Turkey (HPV-vaccine uptake 16.5–26.1% versus 49.4% when having two parents born in the Netherlands), who live in an area with a lower socioeconomic status (HPV-vaccine uptake 36.9% versus 54.8% when socioeconomic status is high) and higher voting proportions in municipalities for Christian political parties (CU&SGP) (HPV-vaccine uptake 41.1% versus 48.5% when voting proportions for Christian political parties are lower) and populist parties with liberal-conservative views (HPV-vaccine uptake 44.8% versus 48.1% when voting proportions for populist parties with liberal conservative views are lower). Besides some changes in political preferences of the population (association between HPV-vaccination uptake and higher voting proportions for populist parties with liberal-conservative views changed with an Adjusted OR (AOR) of 0.86 (95% CI: 0.83–0.90) in 2017 versus 2012) and changes in the association between HPV-vaccination uptake and urbanization level

(the difference in HPV-vaccination uptake between different levels of urbanization becomes smaller) we found no clear determinants which could possibly explain the decrease in the HPV-vaccination uptake.

Several groups in the Netherlands are known to have objections against vaccination in general. Among the orthodox Protestants, who live geographically clustered in the so-called Dutch Bible Belt, approximately 40% has not received childhood vaccinations.[20] In addition, people with affinity with an anthroposophical or natural lifestyle could also have a lower willingness to vaccinate.[21, 22] In our multilevel multivariable logistic regression analysis, we used MMR-vaccination status to indicate people with a lower willingness to vaccinate in general. As expected, we found a significantly lower HPV-vaccination uptake among girls who had not received MMR-vaccinations in the past.

Regarding ethnicity, highest HPV-vaccination uptake was found among girls with both parents born in the Netherlands. Lowest uptake was in particular observed for girls with one or two parents born in Morocco or Turkey. This was also found in a study following the catch-up campaign in the Netherlands.[7] In a systematic review, belonging to minority racial or ethnic groups was also found as risk factors for low completion of HPV-vaccination series.[23] Parents of ethnic groups could be less proficient with the Dutch language and not responding to the invitation. Differences in culture and/ or religion could also explain this association.[24, 25]

Girls living in areas with lower SES appeared to have lower HPV-vaccination uptake than girls living in areas with higher SES. This relation between SES and HPV-vaccination uptake was also shown in a previous study in the Netherlands. [7] Underlying characteristics which play a role in SES are education level, having a paid job and the income of the household. Although vaccination was free of charge, a higher education level will help to better understand the usefulness of HPV-vaccination. In contrast, studies from England, Switzerland and the US showed that vaccination rates were lower in high income families or in families with higher education.[26-28] Differences in healthcare systems and vaccination programs (i.e. school-based) between countries could lead to discrepancies in the association between SES and HPV-vaccination uptake.

In the most recent invitation year, 2017, a road distance to the vaccination location of more than five kilometres showed in the multilevel multivariable logistic regression model a very small but statistically significant association with a lower HPV-vaccination uptake. In contrast, no significant association was found between road distance to vaccination location and HPV vaccination uptake in 2012 and 2014.

Another Dutch study showed that the average road distance was 5.7 km and was comparable between 2014 and 2017.[29] People may have become more critical about travel distance nowadays. So, decreasing the road distance by expanding the number of vaccination locations, especially in rural areas, might help to increase the HPV-vaccination uptake but the magnitude of the effect is uncertain. In countries who have a school-based vaccination program (such as the UK and Australia), in which no additional traveling is necessary, the HPV-vaccination uptake is in general higher.[30]

In 2012 and 2014, girls living in areas with higher urbanization levels had a lower HPV-vaccination uptake than girls living in areas with lower urbanization levels. However, in 2017, this association was not found. The Dutch study performed among girls eligible for the catch-up campaign in 2009 showed that unvaccinated girls lived in more urbanized areas.[9] In contrast, a study from Switzerland, showed that living in a rural municipality was associated with a lower uptake.[27]

Regarding voting proportions in national elections, we found a lower HPV-vaccination uptake in girls living in municipalities with a higher voting proportions for the Christian political parties (CU&SGP), compared to the national mean. The association between high political preference for Protestant Christian parties and low HPV-vaccination uptake was shown before in the Netherlands.[7] Apart from the objections to vaccination in general, various Christian groups have objections to HPV-vaccination in particular, because it concerns protection against a sexually transmitted disease. [7, 9, 31] A study in the US showed that adolescents from households with orthodox religious beliefs were almost 14 times less likely to get vaccinated.[32] In Switzerland, protestant religious groups were also associated with a lower uptake.[27]

Also in 2017, a higher municipal voting proportion for populist parties with liberal-conservative views was found to be associated with a lower HPV-vaccination uptake. Previous database studies found that voters for Party for Freedom (PVV) and Forum for Democracy (FvD) may have less confidence in the government, media, and social institutions.[15, 16] Also, some of the PVV & FvD voters believe that the government hides information about the health risks of vaccines.[15] State-level voting patterns in the US, which may reflect population-level differences in cultural norms and social values, are also associated with uptake for adolescence vaccination.[14]

In birth cohorts 2002 and 2003, i.e. who were vaccinated in 2015 and 2016, a sharp decrease in vaccination uptake was observed.[5] To study which determinants were associated with the decrease in the HPV-vaccination coverage it was investigated whether the influence of the various determinants changed over time. Results showed that the association with urbanization level was less clear in the invitation year 2017,

compared with 2012 and 2014. Also, no association between the municipal voting rate for populist parties with liberal-conservative views was found in 2012 and 2014. However, in 2017 a high percentage of voters for populist parties with liberal-conservative views in the municipality was associated with a lower HPV vaccination uptake. This might be due to the lower confidence in the government, media and social institutions as mentioned before.[15, 16] Besides the changes in political preferences of the population and changes in the association between HPV uptake and urbanization level we found no clear determinants associated with the decrease in the HPV-vaccination uptake. The decrease in HPV vaccination uptake may be more associated with a general decrease in trust in the vaccine and/or the fear of adverse events. Social media might have played a role in this.

Tailored strategies are critical in reaching groups with suboptimal vaccination uptake.[33] We were able to identify target groups that are currently associated with a lower HPV-vaccination rate in the Netherlands. Customized information and/or consultation might be useful to implement for low educated natives, girls with Moroccan or Turkish parents, girls with a Christian background and neighbourhoods with a high proportion of voters for populist parties with liberal-conservative views to increase the HPV-vaccination uptake among these groups. Literature research also shows that reminders (before the vaccination moment), a no-show policy (such as a new invitation if one did not show up after the first invitation), customized information, feedback of the vaccination rate to professionals and making it easier to get the vaccinations, can lead to an increase the HPV-vaccination rate up to 10–20%.[34] Also other studies have been initiated in the Netherlands to reduce the inequalities in HPV-vaccination uptake.[35, 36]

Besides the strength that individual data was used on vaccination status to determine the HPV-vaccination uptake, this study has also some limitations. Data on social, economic, cultural and political determinants were not collected for the purpose of this study and only available on postal code level or municipality level. Therefore, associations on these aggregation levels represent the group of individuals within a given area and might not directly apply to an individual. For example, it concerns the voting behaviour of adults in the municipality, while these girls were not yet allowed to vote themselves. On the other hand, the decision about vaccination is also mostly made by the parents of the girls. Furthermore, for some determinants data was not available for the specific years included in this study. In this case the most recent data was used. Proportions for the political parties in national elections were only available for 2012 and 2017. For road distance, only data was available for 2014 and 2017. Therefore, the results for 2012 and 2014 should be interpreted with caution. Also, we used home addresses obtained in 2018. Girls might have been

moved in the years before, but we think that these movements outweigh each other and therefore had a very small effect on the analyses. Besides that, some variables contained a large number of missings. Especially for ethnicity, which counted low numbers for some categories in all cohorts, especially in 2012 and 2014. This limits the comparability of these variables over time. Besides the investigated determinants, there are other determinants that are possibly associated with the HPV-vaccination uptake. For example, school education or being the oldest girls in the family (i.e. the first who is eligible for HPV-vaccination). Unfortunately, no information on these or other potential determinants was available in the databases.

Conclusions

In this study we identified current social, economic and cultural determinants that are associated with HPV-vaccination uptake for public health relevance. Customized information and/or consultation should be prepared for identified target groups that are associated with a lower HPV-vaccination rate. We found no clear determinants which explain the decrease in the HPV-vaccination uptake. The vaccination coverage recently increased again in the Netherlands [37], probably fostered by the Meningococcal ACWY vaccination campaign for adolescents. This shows that it is possible to increase the vaccination coverage and protect more girls against cervical cancer. This positive message might help to increase the HPV-vaccination coverage in the Netherlands further.

Declarations

Availability of data and materials

All data generated or analysed during this study are included in this published article and its supplementary information files.

Acknowledgements

Thanks to Petra Oomen to provide the data form Praeventis

Funding

This research study was (partially) supported by the research fund of the Dutch National Institute for Public Health and the Environment (RIVM), the Netherlands, for local Public Health Services.

Contributions

AdM analyzed and interpreted the data. TSK prepared a part of the dataset and also interpreted the data. AdM and TSK both contributed in writing and revising the

manuscript. AvL, HdM and WR substantially contributed in the whole study process and they revised the manuscript several times. RA contributed to the statistical analyses. All authors read and approved the final manuscript.

Ethics declarations

The study was approved by the research ethics committee of the Radboud University Nijmegen Medical Centre, Nijmegen, the Netherlands; CMO number 2018/4744. The Præventis data were provided anonymized to the researchers after approval by the registration commission. Therefore the need for consent of the participants was waived off by the research ethics committee of the Radboud University Nijmegen Medical Centre, Nijmegen, the Netherlands. This study was conducted according to the principles of the most recent World Medical Association Declaration of Helsinki and in accordance with the Medical Research Involving Human Subjects Act (WMO).

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Supplementary materials

File S1. Supplementary materials 1. Not included in this thesis. Available online at https://doi.org/10.1186/s12889-021-11897-0

- Table S1.1. Political parties included in the in the Dutch House of Representatives
- Figure S1.1. Seats in the House of Representatives per political party in the Dutch National Elections of 2012 and 2017

File S2. Supplementary materials 2. Partially included in this thesis.

- Model 1.1. Multilevel multivariable logistic regression analysis of invitation year 2012. Table is presented below
- Model 1.2. Multilevel multivariable logistic regression analysis of invitation year 2014. Table is presented below
- Models 2.1-2.14. Multilevel logistic regression analysis of invitation years 2012-2014-2017 including interaction variables. Not included in this thesis. Available online at https://doi.org/10.1186/s12889-021-11897-0

Model 1.1. Multilevel multivariable logistic regression analysis of invitation year 2012 (n=101,715; 99.3% of the girls included in model)

Variable	N	HPV-uptake % [a]	AOR	95% CI	p-value
MMR-vaccination status					<0.001
Zero vaccinations	5334	3.7%	reference	ref.	ref.
One vaccination	3056	28.4%	9.98	8.47-11.75	<0.001
Two Vaccinations	93325	64.3%	45.73	39.61-52.80	<0.001
Ethnicity					<0.001
NL - NL	17182	63.7%	ref.	ref.	ref.
NL - Turkey	350	32.3%	0.29	0.23-0.37	<0.001
Turkey - Turkey	1303	27.9%	0.25	0.22-0.29	<0.001
NL - Morocco	197	36.5%	0.34	0.25-0.46	<0.001
Morocco - Morocco	1268	18.2%	0.15	0.13-0.18	<0.001
NL- Surinam	369	52.8%	0.72	0.58-0.89	0.003
Surinam - Surinam	541	48.6%	0.66	0.55-0.79	<0.001
NL - Ned Antilles/Aruba	185	51.4%	0.87	0.63-1.21	0.401
Ned Antilles/Aruba - Ned Antilles/Aruba	212	23.6%	0.39	0.27-0.55	<0.001
NL - other WC	744	58.5%	0.93	0.79-1.10	0.404
other WC - other WC	430	43.5%	1.24	0.97-1.59	0.093
NL - other NWC	486	58.0%	0.98	0.81-1.20	0.857
other NWC - other NWC	1173	47.6%	0.76	0.67-0.87	<0.001
other WC - other NWC	92	43.5%	0.66	0.42-1.04	0.075
Unknown	77183	61.2%	0.93	0.89-0.96	<0.001
Socioeconomic status [b]					<0.001
Low	17723	51.4%	ref.	ref.	ref.
Low - intermediate	29714	58.8%	1.19	1.14-1.25	<0.001
High - intermediate	38297	62.7%	1.37	1.30-1.43	<0.001
High	15981	65.3%	1.61	1.52-1.70	<0.001
Road distance					0.333
0 km	12689	60.3%	ref.	ref.	ref.
0-5 km	44087	59.3%	1.00	0.96-1.05	0.888
5-10 km	28723	60.6%	1.01	0.96-1.06	0.651
>10 km	16216	60.7%	0.97	0.91-1.03	0.246
Urbanization level [c]					<0.001
Very high	23324	53.2%	ref.	ref.	ref.
High	31670	60.2%	1.04	0.88-1.24	0.623
Moderately high	17138	62.7%	1.08	0.91-1.29	0.383
Low	21108	63.8%	1.31	1.09-1.57	0.004
Very low	8475	63.0%	1.44	1.18-1.75	<0.001

Model 1.1. Multilevel multivariable logistic regression analysis of invitation year 2012 (n=101,715; 99.3% of the girls included in model) (continued)

Variable	N	HPV-uptake % [a]	AOR	95% CI	p-value
Voting % People's Party for Freedom and Democracy (VVD) [d]					
Lower	64075	57.2%	ref.	ref.	ref.
Higher	37640	64.8%	1.21	1.10-1.32	<0.001
Voting % Labour Party (PvdA), Denk (DENK) [d]					
Lower	36335	60.9%	ref.	ref.	ref.
Higher	65380	59.5%	1.13	1.03-1.25	<0.001
Voting % Party for Freedom (PVV), Forum for Democrac y (FvD) [d]					
Lower	57314	59.6%	ref.	ref.	ref.
Higher	44401	60.5%	1.11	1.01-1.21	0.29
Voting % Socialist Party (SP) [d]					
Lower	51984	57.6%	ref.	ref.	ref.
Higher	49731	62.6%	1.31	1.20-1.44	<0.001
Voting % Christian Democratic Appeal (CDA) [d]					
Lower	76857	59.8%	ref.	ref.	ref.
Higher	24858	60.6%	0.89	0.81-0.99	0.003
Voting % Democrats 66 (D66) [d]					
Lower	43093	59.9%	ref.	ref.	ref.
Higher	58622	60.1%	1.08	0.97-1.20	0.145
Voting % Christian Union (CU), Reformed Political Party (SGP) [d]					
Lower	77953	61.8%	ref.	ref.	ref.
Higher	23762	54.3%	0.74	0.66-0.83	<0.001
Voting % Green Left (GL) [d]					
Lower	44304	61.9%	ref.	ref.	ref.
Higher	57411	58.5%	1.06	0.95-1.18	0.320
Voting % Party for the Animals (PvdD) [d]					
Lower	37601	61.8%	ref.	ref.	ref.
Higher	64114	59.0%	0.98	0.88-1.08	0.610
Voting % 50PLUS (50+) [d]					
Lower	57050	58.0%	ref.	ref.	ref.
Higher	44665	62.6%	0.95	0.86-1.04	0.268

Abbreviations: AOR=adjusted odds ratio, CI=confidence interval, MMR=mumps-measles-rubella, NL=the Netherlands, Ned Antilles/Aruba= the Netherlands Antilles and Aruba, WC=western countries, NWC=nonwestern countries, km=kilometre, VVD=People's Party for Freedom and Democracy, PvdA=Labour Party, PVV=Party for Freedom, FvD=Forum for Democracy, SP=Socialist Party, CDA=Christian Democratic Appeal, D66=Democrats 66, CU=Christian Union, SGP=Reformed Political Party, GL=Green Left, PvdD=The Party for the Animals, 50+=50PLUS.

[a] HPV-uptake %= % of total of girls (N) with a completed HPV-vaccination series (2 doses).

[b] Socioeconomic status classification; low (≤-1.0000), low-intermediate (-0.9999 to 0.0000), highintermediate (0.0001-0.9999), high (≥1.0000).

[c] Urbanization classification; Very high: >2500 addresses per km2, high: 1500-2500 addresses per km2, moderately high: 1000-1500 addresses per km2, low: 500-100 addresses per km2, very low <500 addresses per km2

[d] Voting % classification: higher or lower compared to the national mean.

Model 1.2. Multilevel multivariable logistic regression analysis of invitation year 2014 (n=100,430; 99.4% of the girls included in model)

Variable	N	HPV-uptake % [a]	AOR	95% CI	p-value
MMR-vaccination status					<0.001
Zero vaccinations	3181	6.6%	reference	ref.	ref.
One vaccination	3289	26.2%	4.85	4.12-5.70	<0.001
Two Vaccinations	93960	66.0%	26.69	23.15-30.78	<0.001
Ethnicity					<0.001
NL - NL	17655	65.3%	ref.	ref.	ref.
NL - Turkey	404	34.7%	0.31	0.25-0.38	<0.001
Turkey - Turkey	1133	30.3%	0.27	0.23-0.31	<0.001
NL - Morocco	224	35.7%	0.34	0.26-0.45	<0.001
Morocco - Morocco	1249	23.9%	0.21	0.18-0.24	<0.001
NL- Surinam	411	54.7%	0.73	0.60-0.90	<0.001
Surinam - Surinam	463	57.9%	0.90	0.74-1.10	0.302
NL - Ned Antilles/Aruba	161	57.8%	0.76	0.55-1.05	0.097
Ned Antilles/Aruba - Ned Antilles/Aruba	149	45.0%	0.66	0.47-0.95	0.024
NL - other WC	856	64.0%	1.04	0.90-1.22	0.595
other WC - other WC	467	53.1%	1.56	1.24-1.97	<0.001
NL - other NWC	580	60.0%	0.95	0.80-1.14	0.606
other NWC - other NWC	1190	59.3%	1.14	1.00-1.30	0.050
other WC - other NWC	104	44.2%	0.61	0.40-0.92	0.019
Unknown	75384	63.9%	0.96	0.93-1.00	0.064
Socioeconomic status [b]					<0.001
Low	19395	54.9%	ref.	ref.	ref.
Low - intermediate	26556	62.9%	1.26	1.20-1.32	<0.001
High - intermediate	37747	64.4%	1.46	1.39-1.53	<0.001
High	16732	68.4%	1.74	1.65-1.84	<0.001
Road distance					0.232
0 km	13658	62.3%	ref.	ref.	ref.
0-5 km	41275	62.0%	1.00	0.95-1.04	0.914
5-10 km	28363	63.9%	0.99	0.95-1.04	0.796
>10 km	17134	63.3%	0.95	0.89-1.01	0.080

Model 1.2. Multilevel multivariable logistic regression analysis of invitation year 2014 (n=100,430; 99.4% of the girls included in model) (continued)

Variable	N	HPV-uptake % [a]	AOR	95% CI	p-value
Urbanization level [c]					0.001
Very high	19403	57.8%	ref.	ref.	ref.
High	30433	62.9%	1.00	0.83-1.21	0.979
Moderately high	18216	64.0%	1.03	0.85-1.25	0.759
Low	23002	65.6%	1.23	1.01-1.49	0.043
Very low	9376	64.1%	1.31	1.06-1.61	0.014
Voting % People's Party for Freedom and Democracy (VVD) [d]					
Lower	60416	60.5%	ref.	ref.	ref.
Higher	40014	66.4%	1.20	1.09-1.32	<0.001
Voting % Labour Party (PvdA), Denk (DENK) [d]					
Lower	38873	62.7%	ref.	ref.	ref.
Higher	61557	62.9%	1.11	1.00-1.22	0.049
Voting % Party for Freedom (PVV), Forum for Democracy (FvD) [d]					
Lower	56383	62.3%	ref.	ref.	ref.
Higher	44047	63.5%	1.07	0.98-1.18	0.148
Voting % Socialist Party (SP) [d]					
Lower	52884	59.8%	ref.	ref.	ref.
Higher	47546	66.2%	1.47	1.33-1.62	<0.001
Voting % Christian Democratic Appeal (CDA) [d]					
Lower	73453	63.0%	ref.	ref.	ref.
Higher	26977	62.4%	0.93	0.84-1.03	0.176
Voting % Democrats 66 (D66) [d]					
Lower	45487	61.2%	ref.	ref.	ref.
Higher	54943	64.2%	1.15	1.03-1.28	0.016
Voting % Christian Union (CU), Reformed Political Party (SGP) [d]					
Lower	75069	64.9%	ref.	ref.	ref.
Higher	25361	56.7%	0.78	0.69-0.87	<0.001
Voting % Green Left (GL) [d]					
Lower	47508	63.2%	ref.	ref.	ref.
Higher	52922	62.5%	1.04	0.93-1.17	0.499
Voting % Party for the Animals (PvdD) [d]					
Lower	40518	63.7%	ref.	ref.	ref.
Higher	59912	62.2%	0.96	0.86-1.06	0.395
Voting % 50PLUS (50+) [d]					
Lower	55333	61.0%	ref.	ref.	ref.
Higher	45097	65.0%	0.90	0.81-0.99	0.038

Abbreviations: AOR=adjusted odds ratio, CI=confidence interval, MMR=mumps-measles-rubella, NL=the Netherlands, Ned Antilles/Aruba= the Netherlands Antilles and Aruba, WC=western countries, NWC=nonwestern countries, km=kilometre, VVD=People's Party for Freedom and Democracy, PvdA=Labour Party, PVV=Party for Freedom, FvD=Forum for Democracy, SP=Socialist Party, CDA=Christian Democratic Appeal, D66=Democrats 66, CU=Christian Union, SGP=Reformed Political Party, GL=Green Left, PvdD=The Party for the Animals, 50+=50PLUS.

[a] HPV-uptake %= % of total of girls (N) with a completed HPV-vaccination series (2 doses).

[b] Socioeconomic status classification; low (≤-1.0000), low-intermediate (-0.9999 to 0.0000), highintermediate (0.0001-0.9999), high (≥1.0000).

[c] Urbanization classification; Very high: >2500 addresses per km2, high: 1500-2500 addresses per km2, moderately high: 1000-1500 addresses per km2, low: 500-100 addresses per km2, very low <500 addresses per km2

[d] Voting % classification: higher or lower compared to the national mean.

Chapter 3

Risk factors for persisting measles susceptibility: a case-control study among unvaccinated orthodox Protestants

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European Journal of Public Health, 2018;28:922-927

Abstract

Background

Measles is an infectious disease providing lifelong immunity. Epidemics periodically occur among unvaccinated orthodox Protestants in the Netherlands. During the 2013/2014 epidemic, 17% of the reported patients was over 14 years old. Apparently, they did not catch measles during the previous 1999/2000 epidemic and remained susceptible. We wanted to identify risk factors for this so-called persisting measles susceptibility, and thus risk factors for acquiring measles at older age with increased risk of complications.

Methods

A case-control study was performed among unvaccinated orthodox Protestants born between 1988 and 1998; cases had measles in 2013/2014, controls during or before 1999/2000. Associations between demographic, geographical and religion-related determinants and persisting measles susceptibility were determined using univariate and multivariable logistic regression. Analyses were stratified in two age-groups: infants/toddlers and primary school-aged children during the 1999/2000 measles epidemic.

Results

In total, 204 cases and 563 controls were included. Risk factors for persisting measles susceptibility for infants/toddlers in 1999/2000 were belonging to a moderately conservative church, absence of older siblings and residency outside low vaccination coverage (LVC)-municipalities. Risk factors for primary school-aged children were residency outside LVC-municipalities and attendance of non-orthodox Protestant primary school.

Conclusion

Unvaccinated orthodox Protestant adolescents and adults who resided outside the LVC-municipalities, did not attend an orthodox Protestant primary school, had no older siblings and belonged to a moderately conservative church were at risk for persisting measles susceptibility and, thus, for acquiring measles at older age with increased risk of complications. For this subgroup of orthodox Protestants targeted information on vaccination is recommended.

Topics: Adolescent, Adult, Infant, Internship and residency, Netherlands, Relationship – sibling, Vaccination, Measles, Epidemics, Toddler, School-age child, Vaccination coverage

Introduction

Measles is a highly infectious disease that causes high fever, rash, cough and conjunctivitis.[1] Measles provides lifelong immunity; after recovery the patient is not susceptible to measles anymore.[2] In Western countries, measles is no longer considered a childhood disease as it affects adolescents and adults as well.[1, 3] In several European countries a shift towards a higher median age of unvaccinated cases is reported during measles epidemics.[4-6] Measles at higher age is associated with an increased risk of complications such as pneumonia, diarrhoea, acute encephalitis, hepatitis and post-infectious encephalomyelitis, resulting in relatively high hospitalization rates and deaths.[1, 7] Measles can be prevented by vaccination. In the Netherlands measles vaccination has been offered free of charge to all children since 1976. Catch-up vaccination is possible until 18 years and actively offered during epidemics. Before introduction of vaccination, large measles epidemics occurred every other year. Despite a national vaccination coverage of 96% (at the age of two), measles epidemics still occur in the Netherlands.[8] These epidemics are largely confined to an orthodox Protestant minority of 250.000 people with religious objections to vaccination.[7, 9] They are members of various small orthodox Protestant church denominations (OPD), each with varied interpretations of the Bible with respect to vaccination. Vaccination coverage varies between the different OPDs from <15 to >85%.[10] Overall, vaccination coverage among orthodox Protestants is ~60%.[10]

Historically, Dutch orthodox Protestants live in rural areas stretching from the south-west to the northeast of the Netherlands, commonly referred to as the Bible Belt.[11] Nowadays, about 75% of the orthodox Protestants live geographically clustered in this area.[11, 12] In 2013, 29 municipalities in this area had a vaccination coverage <90% [low vaccination coverage (LVC)-municipalities)].[13]

Apart from geographical clustering, strong social clustering is common among orthodox Protestants. Orthodox Protestant families are characterized as large, close-knit families with an average of four children per family, the national average being 1.7. [14, 15] Furthermore, the orthodox Protestant minority has its own political party (SGP), schools, newspaper, magazines, social media platforms and websites. Almost half of the 160 orthodox Protestant primary schools are located in (rural) LVC-municipalities, the others are located in larger towns and cities.[16, 17] The seven orthodox Protestant secondary schools and two colleges are all centrally located to serve orthodox Protestants from a large area.[16] Due to this geographical and social clustering of unvaccinated children, the measles virus is easily transmitted within this minority.

During the 2013–14 measles epidemic 2700 measles cases were notified compared to 3292 cases during the 1999/2000 epidemic.[7, 9] However, underreporting of measles cases is common during outbreaks and epidemics, either because patients do not consult a physician or because physicians do not report all cases to public health authorities.[18] Compared to the 1999/2000 epidemic, the 2013/2014 epidemic showed a considerable higher median age of infection and higher incidence in older age groups.[7] As infection with measles provides lifelong immunity, measles patients born before 1999 must have been susceptible for measles during the 1999/2000 epidemic as well. Apparently, they escaped infection during the 1999/2000 epidemic and were thus persistently susceptible to measles, until they were infected in 2013/2014.

We aimed to identify characteristics of unvaccinated orthodox Protestants associated with persistent measles susceptibility after the 1999/2000 epidemic, and, thus, with increased risk of complications when acquiring measles at older age. Based on these characteristics, targeted information can be developed for unvaccinated orthodox Protestant adolescents and adults who are at increased risk of measles and its complications, in order to make them aware of their susceptibility and consider vaccination. Moreover, knowledge of the characteristics of those with persistent susceptibility can be used for estimating the potential burden of disease, and health care use in future measles epidemics.

Methods

Study design and participants

We performed a retrospective case-control study among unvaccinated orthodox Protestants born between 1988 and 1998. These individuals were 14–26 years of age during the measles epidemic of 2013/2014 and born before the 1999/2000 measles epidemic.

Cases were individuals who were notified with measles during the 2013/2014 epidemic. In the Netherlands measles is a mandatory notifiable disease; laboratory confirmed and epidemiologically linked cases have to be reported to the Regional Public Health Service (RPHS) by physicians and laboratories.[19] All RPHSs that covered one or more LVC-municipalities (12 of the 25 Dutch RPHS regions) participated in this study.

Controls were individuals with self-reported measles (including symptoms of fever, rash, red and watery eyes, rhinitis and/or cough) during or before the 1999/2000 epidemic.

Data-analysis

Based on postal codes, respondents were classified as living in or outside a LVC-municipality. A LVC-municipality was defined as a municipality with a vaccination coverage <90% in 2013 and in which >5% of the population voted for the orthodox Protestant political party (SGP). In 2013, 29 out of 408 municipalities in the Netherlands were LVC-municipalities.[13]

The OPDs were classified into two categories based on level of conservatism and vaccination coverage.[10, 20] OPDs with a high level of conservatism (Old Reformed Congregations and Reformed Congregations in the Netherlands) have a vaccination coverage of <25%. OPDs with a moderate level of conservatism have respective vaccination coverages of 50–75% (Reformed Congregations and Restored Reformed Church), and >85% in Christian Reformed Churches and Protestant Church in the Netherlands, including the Reformed Bond.[10]

For respondents who were school-aged in 1999/2000, the school attendance variable was dichotomized in whether or not they attended an orthodox Protestant school (OPS vs. non-OPS).

Statistical analysis

The main outcome variable was 'persisting measles susceptibility', i.e. not being infected with measles during the 1999/2000 epidemic. Descriptive analyses were conducted using mean and percentages in categorical variables and mean and interquartile range in continuous variables.

As school attendance is known to be strongly associated with childhood infections, analyses were stratified into two age-groups.[21, 22] Group 1 consisted of infants and toddlers born in 1996–98 who were too young to attend school; group 2 consisted of school-aged children born in 1988–95.

Univariate and multivariable logistic regression (OR, 95%CI) was used to determine the association between the main outcome variable 'persisting measles susceptibility' and the determinants: gender, presence of older siblings, residency in LVC-municipalities, OPS attendance and OPD-membership. Determinants that were statistically significantly associated with the outcome variable ($P < 0.05$) in the univariate analysis were included in the multivariable analysis.

Since almost half of the primary OPSs are located in LVC-municipalities, the determinants 'residing in LVC-municipalities' and 'type of school attendance' were combined for the group of school-aged children, resulting in four categories: (i)

residing in a LVC-municipality and attending an OPS, (ii) residing outside a LVC-municipality and attending an OPS, (iii) resident in a LVC-municipality and not attending an OPS and (iv) residing outside a LVC-municipality and not attending an OPS.

All statistical analysis were conducted using SPSS version 21.

Ethics

The study was approved by the research ethics committee of the Radboud University Nijmegen Medical Centre, Nijmegen, the Netherlands; CMO number 2014/1519.

Results

The total study population consisted of 767 persons; 204 cases and 563 controls.

Of the 304 reported measles cases who were invited to participate in the study, 240 responded to the questionnaire (response rate 79%) and 16 questionnaires were incomplete on essential questions— residency and school attendance—and 20 respondents did not meet the inclusion criteria regarding measles, year of birth, vaccination status or church denomination. Accordingly, 204 cases were included (Fig 1). In total 1738 controls responded to the online questionnaire, of which 396 questionnaires were incomplete on essential questions, namely residency and school attendance. The inclusion criteria for controls were not met in 779 questionnaires, most frequently because the respondents did not report having contracted measles as a child or reported to have had measles during the 2013/2014 epidemic instead of the 1999/2000 epidemic. Finally, 563 controls were included for analysis (Fig 1).

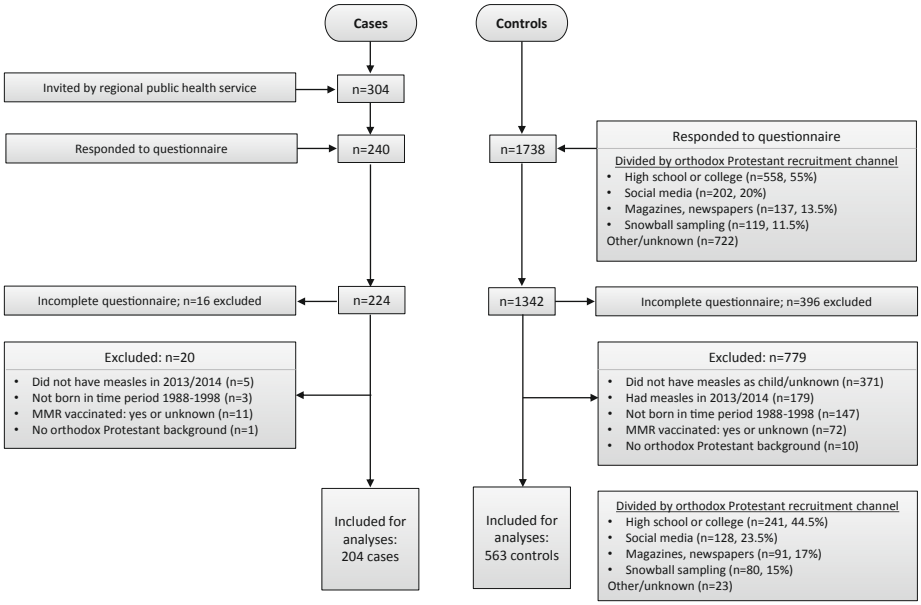

Figure 1. Recruitment and response flowchart of cases and controls (n =2042)

Characteristics of cases and controls are shown in Table 1. Overall, 74% of the respondents included in the study were female. More than half of the controls were school-aged in 1999/2000 (53.1%) compared to one third of the cases (32.3%). Some of the completed questionnaires which were included for data-analysis lacked postal code data due to a technical problem in the online questionnaire. Postal code data of the cases who were included for data-analysis was therefore compared to the postal code data of all reported measles cases who were initially invited by RPHSs. There was no statistically significant difference in residency in a LVC-municipality between invited cases and included cases (resp. 48.2% and 49.3%, P=0.83).

Table 1. Characteristics of unvaccinated orthodox Protestant cases and controls (n=767)

	Total	Cases (n=204)		Controls (n=563)	
Year of birth (IQR)	767	204	1996 (1994-1997)	563	1995 (1991-1997)
Not attending school in 1999/2000 (IQR)	391	134	1997 (1996-1998)	257	1997 (1997-1998)
Attending school in 1999/2000 (IQR)	376	70	1993 (1991-1994)	306	1992 (1990-1994)
	N	**n**	**%**	**N**	**%**
Gender					
Female	564	122	60.4%	442	78.6%
Male	200	80	39.6%	120	21.4%
Current family size					
0-2 siblings	108	29	14.3%	79	14.0%
3-5 siblings	355	108	53.2%	247	43.9%
6-8 siblings	210	46	22.7%	164	29.1%
>8 siblings	93	20	9.9%	73	13.0%
Older siblings					
Yes	518	122	59.8%	396	70.3%
No	249	82	40.2%	167	29.7%
Residency in LVC-municipality (2013/2014)					
Yes	409	94	47.2%	315	57.0%
No	343	105	52.8%	238	43.0%
Residency in LVC-municipality (1999/2000)					
Yes	387	60	43.8%	327	59.8%
No	297	77	56.2%	220	40.2%
Attendance to OPS (1999/2000)					
Yes	285	39	60.9%	246	84.5%
No	70	25	39.1%	45	15.5%
Too young	*391*	*134*		*257*	
Orthodox Protestant church denomination					
High level of conservatism	249	39	20.0%	210	38.5%
Old Reformed Congregations	90	17	8.7%	73	13.4%
Reformed Congregations in the Netherlands	159	22	11.3%	137	25.1%
Moderate level of conservatism	492	156	80.0%	336	61.5%
Reformed Congregations	326	101	51.8%	225	41.2%
Restored Reformed Church	95	37	19.0%	58	10.6%
Christian Reformed Churches	33	10	5.1%	23	4.2%
Protestant Church in the Netherlands, including Reformed Bond	38	8	3.9%	30	5.3%

Abbreviations: IQR: Interquartile range, LVC-municipality, municipality with measles vaccination coverage <90%, OPS: orthodox Protestant school

Group 1: infants and toddlers during the 1999/2000 epidemic

In the group of infants/toddlers (n = 391), there were 134 cases and 257 controls. In both univariate and multivariable logistic regression analysis, risk factors associated with persisting measles susceptibility after the 1999/2000 measles epidemic were: male gender (OR in multivariable analysis 3.75; 95%CI 2.02–6.98; P < 0.001), absence of older siblings (OR 3.36; 95%CI 1.90–5.95; P<0.001), membership of a moderately conservative OPD (OR 4.22; 95%CI 2.30–7.74; P<0.001) and no residency in a LVC-municipality during the 1999/2000 measles epidemic (OR 1.91; 95%CI 1.11–3.27; P=0.019) (Table 2).

Table 2. Risk factors for persisting measles susceptibility in unvaccinated orthodox Protestant infants/toddlers during the 1999/2000 measles epidemic (n=391)

	Total (n=391)	Cases (n=134)		Controls (n=257)		Univariate OR (95% CIs)	p-value	Multivariable ORs (95% CIs)	p-value
	N	n	%	n	%				
Gender									
Female	297	79	59.0%	218	84.8%	reference	<0.001	reference	<0.001
Male	94	55	41.0%	39	15.2%	3.89 (2.40-6.32)		3.75 (2.02-6.98)	
Older siblings									
Yes	274	70	52.2%	204	79.4%	ref		ref	
No	117	64	47.8%	53	20.6%	3.52 (2.24-5.54)	<0.001	3.36 (1.90-5.95)	<0.001
Residency in LVC-municipality (1999/2000)									
Yes	204	47	49.5%	157	63.3%	ref	0.020	ref	0.019
No	139	48	50.5%	91	36.7%	1.76 (1.09-2.84)		1.91 (1.11-3.27)	
Orthodox Protestant church denomination									
High level of conservatism	150	29	22.3%	121	48.6%	ref	<0.001	ref	0.001
Moderate level of conservatism	229	101	77.7%	128	51.4%	3.29 (2.03-5.33)		4.22 (2.30-7.74)	

Abbreviations: LVC-municipality: municipality with measles vaccination coverage <90%

Table 3. Risk factors for persisting measles susceptibility in unvaccinated orthodox. Protestant school-aged children during the 1999/2000 measles epidemic (n = 376)

Total (n=376)		**Cases (n=70)**		**Controls (n=306)**		**Univariate OR (95% CIs)**	**p-value**	**Multivariable OR (95% CIs)**	**p-value**
	N	n	%	n	%				
Gender									
Female	267	43	63.2%	224	73.4%	reference	0.091		
Male	104	25	36.8%	81	26.6%	1.61 (0.92-2.80)			
Older siblings									
Yes	244	52	74.3%	192	62.7%	ref			
No	132	18	25.7%	114	37.7%	0.58 (0.33-1.05)	0.068		
Residency in LVC-municipality (1999/2000)									
Yes	183	13	31.0%	170	56.9%	ref	0.002		
No	158	29	69.0%	129	43.1%	2.94 (1.47-5.88)			
Attendance to orthodox Protestant school (OPS) (1999/2000)									
Yes	285	39	60.9%	246	84.5%	ref	<0.001		
No	70	25	39.1%	45	15.5%	3.50 (1.93-6.35)			
Residency in LVC-municipality attendance to orthodox Protestant school (OPS)									
Residing in LVC-municipality, attending OPS	165	5	12.5%	140	48.8%	ref		ref	
Not residing in LVC-municipality, attending OPS	103	21	52.5%	101	35.2%	5.82 (2.12-15.96)	0.001	5.11 (1.84–14.19)	0.002
Residing in LVC-municipality, not attending OPS	27	7	17.5%	21	7.3%	9.33 (2.7-32.12)	<0.001	8.61 (2.47–29.98)	0.001
Not residing in LVC-municipality, not attending OPS	32	7	17.5%	25	8.7%	7.84 (2.30-26.66)	0.001	6.66 (1.87-23.70)	0.003
Orthodox Protestant church denomination									
High level of conservatism	99	10	15.4%	89	30.0%	ref	ref		
Moderate level of conservatism	63	55	84.6	208	70.0	2.35 (1.15-4.83)	0.017	2.27 (0.84-6.17)	0.108

Abbreviations: LVC-municipality: municipality with measles vaccination coverage <90%; OPS: orthodox Protestant school; OR=odds ratio

Group 2: school-aged children during the 1999/2000 epidemic

Of the 376 school-aged children, 70 were cases and 306 were controls. In univariate analysis residency, school attendance and OPD-membership during the 1999/2000 measles epidemic were associated with persisting measles susceptibility (Table 3).

As interaction was expected, the determinants 'residency in LVC-municipality' and 'school attendance' were also combined into four categories. Compared to respondents who did live in an LVC-municipality and attended an OPS, an increased risk of persisting measles susceptibility after the 1999/2000 epidemic was found in those who did not live in an LVC-municipality (OR 5.11; 95%CI 1.84–14.19; P=0.002), or did not attend an OPS (OR 8.61; 95%CI 2.47–29.98; P=0.001), or both (OR 6.66; 95%CI 1.87– 23.70; P=0.003). In particular, not attending an OPS was associated with the highest risk for persisting measles susceptibility. The association between membership of a moderately conservative OPD and persisting measles susceptibility did not reach statistical significance in multivariable logistic regression analysis (OR 2.27; 95%CI 0.84–6.17; P=0.108).

Discussion

We set out to identify characteristics of unvaccinated orthodox Protestants that were associated with persisting measles susceptibility after the 1999/2000 measles epidemic—i.e. not being infected with measles during this epidemic. Since school attendance is known to be strongly associated with childhood infections, risk factors for persisting measles susceptibility were examined in two age-groups: infants/toddlers and school-aged children. Unvaccinated infants and toddlers who belonged to a moderately conservative church, did not have older siblings and did not live in a LVC-municipality during the 1999/2000 measles epidemic were more likely to remain susceptible for measles. Risk factors for persisting measles susceptibility in unvaccinated school-aged children were not attending an OPS and living outside a LVC-municipality.

Although male gender was found to be statistically significantly associated with persisting measles susceptibility, this is not interpreted as a relevant risk factor, since both sexes are equally affected during measles epidemics.[7, 9] The overrepresentation of females in the study is probably due to a greater interest of women in the subject of health and vaccination, which has been found earlier in comparable studies.[23, 24]

Unvaccinated orthodox Protestants with the identified risk factors may be -unknowingly- susceptible during a new epidemic in their adolescence or adulthood. It

is to be expected that during the 2013/2014 measles epidemic orthodox Protestants—with similar risk factors—were not infected with measles and will still be susceptible for measles during a future measles epidemic. Woudenberg et al. state that an increasing vaccination coverage within the orthodox Protestant minority may be reflected in a longer inter-epidemic period resulting in cases of older age during the subsequent measles epidemic.[7] This emphasizes the importance for these orthodox Protestants to be aware of their susceptibility and of the increased risk of complications when getting infected in adulthood, in order to reconsider vaccination.

A study by Spaan et al. shows that vaccination coverage among orthodox Protestants has increased over the generations, especially in moderately conservative denominations.[24] Also, positive vaccination intention for their children was higher among these respondents. It is possible that these young parents, who do want to vaccinate their children, are still susceptible for vaccine-preventable diseases, such as measles, because they were not infected in their childhood. There are several opportunities for health care professionals to discuss the persisting susceptibility to childhood diseases and the increased risk of complications in adulthood and to offer catch-up vaccination, for instance, when vaccinations are offered to protect against work-related or travel-related diseases. There may also be an opportunity to discuss possible susceptibility and catch-up vaccinations with parents, in consultations during which vaccinations for their children in the National Immunization Program are discussed and provided. As vaccination is a delicate subject for orthodox Protestants, the approach should be focussed on informed decision making, taking into account the risk of persisting susceptibility and, the risk of measles and its complications at adult age.[23, 25]

Our study has several limitations. First, RPHSs could only select reported cases of the 2013/2014 epidemic for recruitment of measles cases. Even though a large underreporting of clinical measles cases during the epidemic was suspected, the participating cases are expected to be sufficiently representative. Given that the main study determinants—e.g. residency in LVC-municipality and school attendance as child—do not influence visiting a GP when having measles as adolescent or adult, it is not expected that underreporting of cases by GPs has affected the outcome of this study.

Second, it was not possible to select a random sample of unvaccinated orthodox Protestant controls, since in the Netherlands religion is not recorded in public registrations. Therefore, data collection methods were used which have been found successful in this population in the past.[10, 24, 25] For the recruitment of controls, school boards of orthodox Protestant secondary schools were involved,

which resulted in a high response rate. However, we had to exclude a high number of questionnaires for data-analysis since the school boards invited every student of the birth cohorts 1988–98, including vaccinated students and students who were infected with measles in 2013/2014 (Fig 1). We presume that this does not influence the study results.

Third, controls self-reported their measles virus infection during childhood and based on their background as unvaccinated orthodox Protestants it is highly probable that they did have measles as child. It is, however, possible that we included controls who did not have measles as a child, which may have diluted the differences between cases and controls. Nevertheless, this misclassification would have resulted in an underestimation rather than overestimation of associations.

Furthermore, involving orthodox Protestants secondary schools in the recruitment of controls could have resulted in selection bias concerning the risk factors 'attendance to an orthodox Protestant primary school' and 'residency in LVC-municipalities'. However, orthodox Protestant secondary schools are centrally located and serve both students from LVC- and non-LVC-municipalities and these secondary schools are not connected to orthodox Protestant primary schools. Moreover, most respondents attending these secondary schools were too young to go to primary school during the 1999/2000 epidemic.

Conclusion

In this study we identified risk factors of persisting measles susceptibility among unvaccinated adolescents and young adults within an orthodox Protestants community following a measles epidemic in their childhood. These risk factors included not attending an OPS and not living in a LVC-municipality during the childhood measles epidemic. For those who were too young to attend school, not having older siblings and belonging to a moderately conservative church denomination were additional risk factors. Since this specific group of moderately conservative orthodox Protestants may also be more open to discuss the subject of vaccination, they should be informed about these risks and offered catch-up vaccination.

Declarations

Acknowledgements

We thank the orthodox Protestant secondary schools (Van Lodenstein College, Driestar College and Driestar Educatief) for their assistance with the recruitment of controls among their students. Furthermore, we thank all participants for completing

the study's questionnaire. We would also like to thank Toos Waegemaekers for her contributions to the research proposal.

Funding

This work was financially supported by the Program for Strengthening Control of Infectious Diseases by Municipal Health Services of the National Institute for Public Health and the Environment (RIVM), the Netherlands.

Conflicts of interest

None declared

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Chapter 4

Considerable doubt about rubella screening and vaccination among unvaccinated orthodox Protestant women: a mixed-methods study

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BMC Public Health, 2023;23:693

Abstract

Background

Women who are susceptible to rubella are advised to vaccinate against rubella to prevent infection in future pregnancies, and thus avert the risk of congenital rubella syndrome in their unborn child. Rubella outbreaks periodically occur in the under-vaccinated orthodox Protestant community in the Netherlands. The objective of this mixed-methods study was to determine and understand personal experience with rubella, perceived rubella susceptibility, and intention to accept rubella screening and vaccination among unvaccinated orthodox Protestant women. The ultimate aim of this study was to inform policy and practice and contribute to the prevention of cases of congenital rubella syndrome.

Methods

A mixed-methods study was conducted using an online survey and semi-structured interviews among unvaccinated orthodox Protestant women aged 18-40 years. Descriptive analysis was used for quantitative data. Qualitative data was analysed using codes and categories.

Results

Results of the survey (167 participants) showed that most participants had personal experience with rubella (74%, 123/167) and 101 women (61%, 101/167) indicated they had had rubella themselves. More than half of the women were undecided whether to accept rubella susceptibility screening (56%; 87/156) or rubella vaccination (55%; 80/146). Qualitative findings (10 participants) showed that most women thought they were unsusceptible to rubella. Indecisiveness and negative attitudes to accept rubella vaccination were related with religious arguments to object vaccination and women's perception of absence of imminent threat of rubella. Furthermore, results showed presence of misconceptions among women in the interpretation of their susceptibility and high confidence in their parents' memory that they had experienced rubella as a child although no laboratory screening had been conducted.

Conclusions

In light of an imminent rubella outbreak in the Netherlands, a tailored education campaign should be prepared aimed at and established in cooperation with the under-vaccinated orthodox Protestant community. Health care providers should provide adequate information on rubella and support decision-making in order to stimulate women to make a deliberate and informed decision on rubella screening and, if necessary, subsequent vaccination.

Keywords: Decision making; Intention; Vaccine hesitancy; Health Personnel; Religious belief

Introduction

Rubella is a highly contagious, yet, generally non-severe disease that passes with mild or no symptoms.[1] However, rubella infection during pregnancy, particularly in the first trimester, can result in miscarriage and stillbirth, and/or cause severe complications in the developing fetus, known as congenital rubella syndrome (CRS). CRS is characterised by ophthalmological, cardiac, brain, genitourinary and other abnormalities, including hearing loss and low birth weight.[2] Many countries offer rubella vaccination to all children in vaccination programmes, often in a combination vaccine, e.g. measles-mumps-rubella (MMR-)vaccination.[3, 4] In the Netherlands, children are offered two MMR-vaccinations at the ages of 14 months (MMR1), and 9 years (MMR2).[5] Both vaccination and natural infection provide lifelong immunity against rubella [4].

To eliminate rubella, countries need a high vaccination uptake. In countries with a near-optimal vaccination coverage, the incidence of rubella is reduced, however, the disease is not eliminated. In these countries, longer time periods between rubella outbreaks may be observed, increasing the average age of infection and making it an adult disease as well.[6] For this reason, children are born with CRS in countries with successful vaccination programmes. Despite the goal to eliminate rubella in the WHO European region, 27 CRS cases have been reported in Italy, and seven in both Spain and Portugal in the last 15 years.[7]

CRS can be prevented by providing rubella vaccination to susceptible women of childbearing age. Since women who are still susceptible to rubella are rarely registered as such in a national registration system, rubella susceptibility screening is offered to pregnant women during antenatal care.[8] As the live attenuated rubella vaccine is contraindicated during pregnancy, vaccination to susceptible women can only be provided after pregnancy. Many European countries that provide rubella susceptibility screening programmes target all pregnant women, independent of their immunity status.[8] In the Netherlands, national guidelines advise health care providers (HCPs), e.g. midwives, gynaecologists and general practitioners, to offer screening to unvaccinated women and women with an unknown vaccination status during pregnancy.[9, 10]

In 2021, the Netherlands had a first dose MMR-vaccination coverage of 93% among young children, and a second dose MMR-vaccination coverage of 90% among adolescents.[11] Part of those who are not MMR vaccinated during childhood, belong to the orthodox Protestant minority; a socially and geographically clustered close-knit community with low vaccination coverage due to religious objections.[12-14] Today,

the orthodox Protestant community consists of approximately 250.000 persons; ~1.5% of the Dutch population.[15] Roughly three-quarters of the orthodox Protestants live geographically in the so-called Dutch Bible belt, which stretches from the south-west to the north-east of the Netherlands. The most recent large rubella outbreak among this community occurred in 2004-2005, counting 387 reported cases and 11 cases of CRS.[12] No cases of CRS have been reported since this outbreak.[16]

Shortly after the 2004-2005 rubella outbreak in the Netherlands, a small study established a low rubella screening uptake and high rubella seroprevalence among unvaccinated adolescent females in a municipality with a high number of orthodox Protestants.[17] Seroprevalence data from 2016-2017 (epidemiology department of the National Institute for Public Health and the Environment) among 137 orthodox Protestant women aged 18-40y showed that 4% (n=5) were susceptible to rubella; data among 54 orthodox Protestants girls aged 2-17y showed that 30% (n=16) were susceptible to rubella. This indicates a higher susceptibility among the upcoming generation of orthodox Protestant pregnant women. As known from previous studies among orthodox Protestant women, most women want to make an informed and deliberate vaccination decision, with both religious and health-related aspects influencing their vaccination decision.[18, 19] However, more knowledge is needed on orthodox Protestant women's rubella screening and vaccination intention and its underlying mechanisms. This information can then be used in developing policy to reduce health risks.

A mixed-methods study among unvaccinated orthodox Protestant women was set out using a quantitative approach to determine women's personal experience, perceived susceptibility for rubella, and their intention of participation in rubella screening and vaccination. Additionally, a qualitative approach was used to explore and understand the underlying mechanisms of women's perceived susceptibility, and rubella screening and vaccination intention. The ultimate aim of this study is to contribute to the prevention of future CRS cases by informing HCPs and policymakers on how to improve rubella screening and rubella vaccination decision-making support for unvaccinated orthodox Protestant women.

Methods

In 2017-2019 a cross-sectional online survey study and a semi-structured interview study were conducted among Dutch women who were unvaccinated against rubella, aged 18-40 years, who had an orthodox Protestant background. This mixed-methods study was part of a larger research project on vaccine decision-making on vaccine-preventable diseases during pregnancy among orthodox Protestant women.[20]

In the quantitative study, we aimed to include a representative sample of unvaccinated orthodox Protestant women regarding education level, orthodox Protestant church denomination, and residency in an orthodox Protestant municipality. Questionnaires for the survey study were completed between October 2018 and January 2019. Women were recruited to participate through midwife/obstetrical practices, orthodox Protestant (social) media, an orthodox Protestant university of applied science, and key persons (individuals with close contacts in the orthodox Protestant community) in the Netherlands. Means of communication for recruitment were flyers, posters, and online banners referring women to the study's website with a link to the online questionnaire.

Ten questionnaire items on MMR-vaccination status, age, postal code, level of education, church denomination, relationship status, pregnancy status, and having children were previously used in other studies among the orthodox Protestant community and based on expert knowledge.[21, 22] For this study, we added items on personal experience with rubella, perceived susceptibility for rubella, and intention to participate in rubella screening and rubella vaccination. Women were asked about their personal experience with rubella using five answer categories: I have had rubella myself, one or more of my children have had rubella, in my immediate surroundings someone has had rubella, no one in my immediate surroundings has had rubella, and unknown. Participants who were pregnant and participants with children were asked if they perceived themselves to be susceptible to rubella using the answer categories: not susceptible, susceptible, or I do not know.

In answering the question to score their rubella screening intention, all participants were asked to imagine to be offered screening before a desired pregnancy. Additionally, when next scoring their MMR-vaccination intention, all participants were asked to imagine to be still susceptible to rubella. A four-point Likert scale was used to score participants screening intention and the intention to vaccinate: will certainly not accept, will probably not accept, will probably accept, will certainly accept, or unknown/not applicable.

The semi-structured interviews were conducted between March and August 2017. Participants were recruited using purposeful sampling through key persons and snowball sampling. The interviews were held at the participants' homes by trained female interviewers (AdM, DvN and WR). To ensure interviews were conducted in a similar way to reduce bias, the first five interviews were conducted by interviewers AdM and DvN together. In addition, the same interview guide was used for all interviews. The topic guide included open-ended questions about personal experience with rubella, personal experience with rubella during pregnancy,

perceived susceptibility to rubella during pregnancy, and perceived need for protection against rubella, including vaccination.

In the questionnaire and during the interviews, participants did not receive additional information about rubella, screening and vaccination. Therefore, participants' answers were based on their basic knowledge on these topics. Interviewees were also invited to complete a questionnaire. Participants' vaccination status is based on personal report among both interview and survey participants.

Data analysis

Data analysis started with the descriptive analysis of the quantitative survey data using IBM SPSS Statistics 25. Participants who were vaccinated against rubella, women who did not have an orthodox Protestant background, and women who did not reach the final page of the questionnaire were excluded from analysis. Based on their postal code, participants were classified as living or not living in an orthodox Protestant municipality. Orthodox Protestant municipalities were defined as municipalities with at least 5% votes for the orthodox Protestant political party, the Staatkundig Gereformeerde Partij (SGP) in the Dutch National Elections for seats in the House of Representatives in 2021.[23] Qualitative data analysis was conducted using the software program ATLAS.ti 9.1.6. Interviews were recorded with a digital voice recorder and transcribed verbatim. Transcripts were analysed using a thematic content analysis approach. Transcripts were coded, and codes were combined into categories. Subsequently, categories were linked to the four main themes of the survey: personal experience with rubella, perceived susceptibility to rubella during pregnancy, intention to accept rubella screening, and rubella vaccination intention.

Results

One hundred sixty-seven orthodox Protestant women completed the online questionnaire. Among the survey participants, 162 women reported to be unvaccinated against rubella and five women reported an unknown rubella vaccination status. Survey participants were on average 27.3 years old, had a moderate or high education level (56.3% and 36.5%, respectively), 77.8% had a partner or husband, and 65.4% had children and/or was pregnant.(Table 1) Twenty-nine percent (29.3%) was member of a highly conservative church, 59.9% was member of a moderately conservative church, and 10.8% was member of a church with a low level of conservatism. Ten women participated in an interview. All participating women were married and nine women were pregnant and/or had children.(Table 2) The interviewees were member of various orthodox Protestant church denominations.

Table 1. Sociodemographic and rubella related variables of unvaccinated orthodox Protestant survey participants (n=167)

	Mean	Range
Age (in years)	27.3	18-40
Level of education	**N**	**%**
Low [x]	12	7.2%
Moderate [+]	94	56.3%
High [#]	61	36.5%
Church denomination		
High level of conservatism [a]	49	29.3%
Moderate level of conservatism [b]	100	59.9%
Low level of conservatism [c]	18	10.8%
Living in an orthodox Protestant municipality (n=164)		
Yes, living in a municipality with ≥5% votes for SGP*	132	80.5%
No, living in a municipality with <5% votes for SGP*	32	19.5%
Relationship status		
Partner/husband	130	77.8%
No partner	37	22.2%
Has children and/or is pregnant (n=162)		
Yes	106	65.4%
No	56	34.6%
Personal experience with rubella (multiple responses possible)		
“Yes, I have had rubella myself”	101	60.5%
“Yes, my child(ren) has/have had rubella”	9	5.4%
“Yes, somebody close has had rubella”	40	24.0%

Table 1. Sociodemographic and rubella related variables of unvaccinated orthodox Protestant survey participants (n=167) (continued)

	Mean	Range
"No, I do not have any personal experience with rubella"	44	26.3%
Perceived own rubella susceptibility during pregnancy (n=110) *Women who were pregnant and/or with children during survey study*		
Unsusceptible	76	69.1%
Susceptible	8	7.3%
I do not know	26	23.6%
Screening intention (n=156)		
Will certainly refuse screening	36	23.1%
Will probably not accept screening	47	30.1%
Will probably accept screening	40	25.6%
Will certainly accept screening	33	21.2%
Vaccination intention (n=146)		
Will certainly refuse vaccination	60	41.1%
Will probably not accept vaccination	59	40.4%
Will probably accept vaccination	21	14.4%
Will certainly accept vaccination	6	4.1%

Abbreviation: SGP = Staatkundig Gereformeerde Partij (Reformed Political Party)

x No, primary, prevocational, intermediate secondary or lower vocational, or lower professional education

+ Intermediate vocational education, higher secondary education or pre-university education

Higher professional education or scientific education

a Reformed Congregations in the Netherlands (GGiN) or Old Reformed Congregations (OGG)

b Reformed Congregations (GG) or Restored Reformed Church (HHK)

c Christian Reformed Churches (CGK) or Reformed Bond (within Protestant Church in the Netherlands)

* Voting proportion for the SGP in the Dutch National Elections for seats in the House of Representatives in 2021

Table 2. Characteristics of unvaccinated orthodox Protestant interview participants (n=10)

Age (in years), **range**	23-34
Church denomination, n	
High level of conservatism [a]	4
Moderate level of conservatism [b]	5
Low level of conservatism [c]	1
Living in an orthodox Protestant municipality, n	
Yes, living in a municipality with ≥5% votes for SGP*	6
No, living in a municipality with <5% votes for SGP*	4
Relationship status, n	
Husband	10
No husband	0
Has children and/or is pregnant, n	
Yes	9
No	1

Abbreviation: SGP = Staatkundig Gereformeerde Partij (Reformed Political Party)

a Reformed Congregations in the Netherlands (GGiN) or Old Reformed Congregations (OGG)

b Reformed Congregations (GG) or Restored Reformed Church (HHK)

c Christian Reformed Churches (CGK) or Reformed Bond (within Protestant Church in the Netherlands)

* Voting proportion for the SGP in the Dutch National Elections for seats in the House of Representatives in 2021

Personal experience with rubella

Almost three quarters of the participants in the survey study (73.7%) reported a personal experience with rubella. Most experienced rubella themselves (60.5%), or had someone in their direct surroundings who had experienced rubella (24.0%). In the interviews, women recalled having experienced rubella outbreaks in the past but did not consider it as something happening at present. One woman, who thought she might still be susceptible, had been in close contact with ill family members at a birthday party during her pregnancy and could have possibly been infected with rubella.

"I heard later that it was rubella, so I was infected anyway, so there was really nothing I could have done about it." (Interview 6)

Perceived rubella susceptibility

Among the unvaccinated women who were pregnant and/or had children (n=110), 76 (69.1%) considered themselves to be unsusceptible to rubella, 23.6% were unsure about being susceptible, and eight women (7.3%) considered themselves to be

susceptible to rubella. Of the 76 who considered themselves to be unsusceptible, 20 women reported they had not had rubella themselves. Of the eight women who considered themselves to be susceptible, two women reported they had had rubella themselves. This indicates that about a quarter of the participants did not know that immunity is acquired by either rubella vaccination or natural infection. In the interviews, five women who did not receive rubella screening (5/8) clarified they were certain they were immune to rubella, because their parents had told them they had had rubella or 'all of the childhood diseases' as children.

"My mother wrote them (childhood diseases) *all down in a booklet. [...] You just got ill and that was part of it, you had measles or you had rubella and then you were happy, then everyone was happy that you had had it, because then you had antibodies."* (Interview 7)

Rubella screening intention

More than half of the survey participants (55.8%) were undecided whether they wanted to be screened for rubella susceptibility; 30.1% would probably refuse and 25.6% would probably accept screening. Of the others, 23.1% would certainly refuse and 21.2% would certainly accept screening. Among the interviewees, only two women (2/10) indicated that they had been screened for rubella susceptibility during their pregnancy. Both women were screened at the initiative of their midwife. None of the interviewees had actively requested for screening themselves. Strikingly, some women were uncertain whether their midwife screened them during their pregnancy.

"I think that's what you get checked for, at the beginning of the pregnancy. And I think that what came out of it (the screening), *that I had had that* (rubella)*."* (Interview 1)

Rubella vaccination intention

Comparable to screening intention, 54.8% of the survey participants were undecided whether they would accept vaccination if they were susceptible; 40.4% would probably refuse, and 14.4% would probably accept vaccination. While 41.1% would certainly refuse rubella vaccination, only 4.1% would certainly accept rubella vaccination. In the interviews, in line with women's negative attitude towards rubella screening, none of the unvaccinated women would actively request for vaccination. Religious reasons for not doing so were: 'I trust that God protects us', 'God has a purpose for what happens to us in life', and 'As a human being you should not want to be in control of the future'. Non-religious reasons were: 'There is currently no rubella outbreak going on', 'It does not feel as an urgent problem which needs to be solved', and 'I have had all of the childhood diseases'.

"If you would often read it is very dangerous to have rubella in your pregnancy. For example: 'If you are not vaccinated, do it'. Then you would think about it. But not now." (Interview 13)

One woman said she would be more motivated to receive vaccination if someone close had have a child affected by a rubella infection during pregnancy. Several interviewees expected they would like to receive information and/or would like to read information about rubella and necessary precautions if there were a rubella outbreak. Especially women who thought they were or might be susceptible to rubella mentioned taking preventive measures if they were pregnant during a rubella outbreak, such as avoiding high-risk locations (primary schools or households with rubella cases).

"If I were expecting and they had rubella, I wouldn't go there. Because that can just be really harmful to your baby". (Interview 4)

Discussion

This study provides new information on personal experience with rubella, perceived rubella susceptibility, and rubella screening and vaccination intentions among unvaccinated women of childbearing age in a religious minority group. Most unvaccinated orthodox Protestant women indicated they are familiar with rubella and most women thought they are not susceptible to rubella. However, study results showed that this perceived unsusceptibility is rarely confirmed with laboratory screening. The study showed high indecisiveness and negative attitudes to accept rubella screening or rubella vaccination among survey participants. Qualitative study results revealed religious arguments to object vaccination and women's perception of absence of imminent threat of rubella, which could partially explain the low screening and rubella vaccination intention.

Concerning women's perceived susceptibility, the interview outcomes showed that most women rely on their parents' memory whether they had had rubella as a child. Whether it actually was rubella or a similar childhood disease remains largely unknown as only few interviewees received rubella screening during pregnancy. Evidence that self-reported history of rubella is not always reliable is also shown in a Japanese study among HCPs.[24] Among the unvaccinated HCPs who remembered a history of rubella, 5% did not have rubella antibodies. On the other hand, among unvaccinated HCPs who did not remember having a history of diseases, 62% did have rubella antibodies. In our study, it appeared that not all unvaccinated participants understood that immunity was related to natural infection. A quarter (20/76) of the

unvaccinated women who thought they were not susceptible to rubella reported they had not had rubella themselves.

A high degree of the unvaccinated participants was undecided about accepting rubella screening and interviewees showed reluctance to take the initiative to be screened. In Japan, the government provides voluntary-based rubella susceptibility screening and vaccination for adults to eliminate rubella. A study showed that the uptake among women of childbearing age in Japan remains low: only 39% had taken precautionary actions related to rubella prevention.[25] In these women, the main drivers to take action (i.e., checking documented vaccination history, taking rubella antibody screening, or getting vaccinated) were: 1) having knowledge about rubella screening, rubella outbreaks and CRS, 2) having acquaintances who had taken preventive measures, and 3) having a positive attitude towards vaccination. [25] The first driver was found among our interview participants as well. Women mentioned they wanted to gain knowledge on rubella during an outbreak to be able to prevent rubella infection during pregnancy. The second driver is also likely to apply to orthodox Protestants, although it is likely that rubella is a less discussed topic among friends and family members since the last outbreak occurred more than 15 years ago. Moreover, in line with the third driver, orthodox Protestant women's negative attitude can be partially explained by their indecisiveness or negative intention towards vaccination based on both religious and health-related aspects [18, 19], supplemented by their perception that they had been infected with rubella as a child.

More than half of the survey participants was undecided whether they wanted to receive rubella vaccination. An argument underlying this doubt was women's perception that rubella is not an imminent problem as they did not regard rubella as a currently common disease. Karafillakis et al. (2017) found that low risk perception of contracting a vaccine-preventable disease is a frequently mentioned concern in vaccine decision-making, that may outweigh perceived benefits to accept vaccination.[26]

In a previously conducted study on maternal pertussis vaccination, orthodox Protestant women reported gathering information as an essential need to make a well-considered vaccination decision.[18] In addition to receiving information, women in the maternal pertussis vaccination study wanted sufficient time to search for information themselves, to converse with others about the vaccination, and to deliberate the values they consider to be important concerning the vaccination.[18] It can be assumed that unvaccinated women, when offered rubella screening or vaccination, also need both information and sufficient time to come to a deliberate, informed decision.

The COVID-19 pandemic occurred after data collection for this mixed-methods study. During the pandemic, COVID-19 vaccination uptake was lower in orthodox Protestant municipalities in the Netherlands.[27] This lower uptake was influenced by religious arguments, anti-vaccination sentiments and anti-government sentiments.[28] As these sentiments might also impact the vaccination coverage for other vaccinations, increasing the risk for future infectious disease outbreaks including rubella, it is important to monitor the influence of anti-vaccination sentiments on vaccination uptake in follow-up research.

A strength of this study was the combination of quantitative and qualitative data that enabled us to determine women's perceived susceptibility, and rubella screening and vaccination intention, and to understand the underlying mechanisms that support their perspectives. The quantitative study sample was found to be representative for the unvaccinated members of the orthodox Protestant community. Consistent with what we know of unvaccinated orthodox Protestants, our participants were also more often member of a moderately or highly conservative church denominations and more often residing in orthodox Protestant municipalities, compared to the overall orthodox Protestant community.[15] Concerning representativeness of education level, we followed the trend of national statistics among Dutch women [29], which revealed that women with a low level of education were underrepresented in our sample. Previous research among the orthodox Protestant community is not conclusive whether education level is associated with vaccination intention and indecisiveness in vaccination intention.[21, 22] Therefore, we cannot interpret if the underrepresentation of respondents with a low level of education led to outcome bias on the intention to accept rubella vaccination. The purposeful sampling method in the qualitative study resulted in a small, yet, varied sample of age, church denomination and residency in orthodox Protestant municipalities. Level of education was not verified with interview participants, therefore it is unknown whether there is sufficient variation regarding education level in this sample. Finally, both the quantitative and qualitative studies were conducted among a specific under-vaccinated group, namely Dutch orthodox Protestant women, thereby diminishing the applicability of the results to other under-vaccinated groups.

Conclusion and recommendations

This study indicates that half of the unvaccinated orthodox Protestant study participants is undecided whether or not to accept rubella screening and vaccination. This indecisiveness is likely to be related to women's unconfirmed assumptions that they are not susceptible to rubella and their perceived low risk of contracting rubella due to the absence of an outbreak. To prevent CRS cases in future rubella outbreaks,

several recommendations can be made. Firstly, unvaccinated pregnant women and women of childbearing age should be made aware by e.g. national and regional public health institutes that they possibly are susceptible to rubella, which puts their unborn child at risk for CRS. In light of an imminent rubella outbreak in the Netherlands, a tailored education campaign should be prepared aimed at and established in cooperation with the under-vaccinated orthodox Protestant community, as they are most at risk of rubella infection. Secondly, Dutch HCPs involved in (pre)pregnancy care should be reminded to follow guidelines recommending rubella screening to unvaccinated women in order to assess their rubella susceptibility status. HCPs should explain the added value of laboratory screening if women think they have had rubella as child, as rubella can be mistaken for another childhood disease that causes a rash. Thirdly, all HCPs involved in the care of these women should note that they should support these women in their decision-making to enable them to make their own deliberate and informed decision on rubella screening and, if necessary, subsequent vaccination.

Declarations

Ethics approval and consent to participate

The Medical Ethics Committee (CMO) of the Arnhem-Nijmegen region assessed both the qualitative and quantitative study, and concluded that both were exempt from their approval (reference no. quantitative study: 2018-4680, qualitative study: 2017–3178). Written informed consent to participate in the study was obtained from participants before the start of the interview. Interview transcripts were anonymised and untraceable to individuals. Survey participants were asked for consent to participate anonymously at the beginning of the online questionnaire.

Consent for publication

Not applicable.

Data availability

The datasets generated and/or analysed during the current interview study are not publicly available as the raw interviews and transcripts contain sensitive information and study participants are part of a close-knit community, even anonymized raw data can seriously compromise their confidentiality, but are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

The large research project on vaccine decision-making in the orthodox Protestant community about vaccine preventable diseases during pregnancy – of which this mixed-methods study was a part- was supported by the research fund of the National Institute for Public Health and the Environment (RIVM), the Netherlands, for local Public Health Services. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Authors' contributions

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. Author AdM collected most of the interview and survey data. HR and JH assisted in data collection. AdM analysed and interpreted the data, supervised by MH, JH, HR and RR. All authors contributed to the writing of the manuscript and approved the final manuscript.

Acknowledgements

We would like to show our gratitude to all women who participated in this study and the key persons for their assistance in the recruitment of participants. We would like to thank D. van Nimwegen for her assistance in the interviews and M. van de Kam for conducting a literature search. We would like to thank Abigail Sunderland of the Dutch National Institute for Public Health and the Environment for her cooperation in providing the 2016/2017 seroprevalence data.

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Chapter 5

Decision-making on maternal pertussis vaccination among women in a vaccine-hesitant religious group: stages and needs

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PLOS ONE, 2020;15 eCollection 2020

Abstract

Introduction

As of December 2019, pregnant women in the Netherlands are offered pertussis vaccination to protect their newborn infant against pertussis infection. However, the manner in which pregnant women decide about this maternal pertussis vaccination is largely unknown. The aim of this study is to gain insight into the decision-making process regarding maternal pertussis vaccination, and to explore the related needs among the vaccine-hesitant subgroup of orthodox Protestant women.

Methods

Charmaz's grounded theory approach was used to develop a decision-making framework. To construct this framework we used an explorative multimethod approach in which in-depth interviews and online focus groups were supplemented by a literature search and research group meetings. This study was carried out in a hypothetical situation since the maternal pertussis vaccination had yet to be implemented in the Dutch immunisation programme at the time of the study.

Results

Twenty-five orthodox Protestant women participated in an interview, an online focus group, or in both. The findings of this study resulted in a decision-making framework that included three stages of decision-making; an Orientation stage, a value-based Deliberation stage, and Final decision stage. The Orientation stage included the needs for decision-making categorised into Information needs and Conversation needs. Women indicated that -if they were to receive sufficient time for Orientation and Deliberation- they would be able to reach the stage of Final decision.

Conclusion

The decision-making framework resulting from our findings can be used by health care professionals to provide women with information and consultation in the decision-making process. Future studies should investigate whether the stages of and needs for decision-making can be found across other vaccine-hesitant subgroups and vaccinations.

Introduction

Pertussis is a highly contagious respiratory disease, characterized by severe coughing spells.[1, 2] Especially in young infants, pertussis can cause complications such as pneumonia, apnoea, and respiratory failure.[3] Pertussis vaccination is offered in most childhood vaccination programmes. However, the effectiveness of the acellular pertussis vaccine wanes over time, resulting in an increase of pertussis incidence in countries using this pertussis vaccine.[4, 5] The increasing pertussis incidence is most threatening for newborn infants, who are too young to be fully vaccinated.

Since maternal pertussis vaccination is a highly effective, safe and cost-effective intervention to prevent pertussis in newborn babies, many countries recommend pertussis vaccination for pregnant women.[6-8] However, regardless of the general public and individual health benefits of the maternal pertussis vaccine, in various countries which provide maternal pertussis vaccination for pregnant women, health care professionals (HCPs) and governments are confronted with parents' vaccine hesitancy and lower vaccine uptake among pregnant women than expected.[9-12] Providing information and education on the maternal pertussis vaccination does not seem to be sufficient in addressing these women's doubts, as hesitance remains after being informed by an HCP.[13, 14]

As of December 2019, the maternal pertussis vaccination is included in the Dutch immunisation programme. However, in the Netherlands, similar to other Western countries, various groups of people question or refuse vaccinations due to ideological, philosophical or religious beliefs.[15-19] One of these vaccine-hesitant groups is the Dutch orthodox Protestant community which comprises 1.5% of the Dutch population. This community has a long history of vaccine hesitancy as, since the introduction of vaccinations in the 19th century, orthodox Protestants have raised religious objections to vaccinations.[20] Research findings indicate that orthodox Protestant parents make a well-considered decision about childhood vaccinations and do not consider accepting vaccinations as self-evident.[18] Childhood vaccination coverage in this community ranges between 11% and 86%, depending of which specific church denomination orthodox Protestants are member of.[21, 22]

The hesitance towards vaccination in general and maternal pertussis vaccination in particular underlines the importance of shaping the decision-making process in such a way that the information and decision support needs of vaccine-hesitant parents are taken into account.[23-25] Hitherto, however, little is known about vaccine-hesitant parents' needs regarding decision-making on maternal pertussis vaccination.[11, 26-28]

The aim of this study is to gain insight into the decision-making process on the newly introduced maternal pertussis vaccination, and the related needs among a vaccine-hesitant group, namely Dutch orthodox Protestant women. This knowledge can then be used by HCPs to optimize their assistance and support and may contribute to less hesitancy regarding the maternal pertussis vaccination among this specific group of women.

Methods

Research design

To explore the decision-making process and related needs of the participating women, a qualitative research design following Charmaz's grounded theory approach was used to develop an analytic framework of the orthodox Protestant women's decision-making process regarding maternal pertussis vaccination (Fig 1).[29] Methodological triangulation, including interviews, online focus groups (OFGs), a literature search and research group meetings, was applied to increase the validity of the data.[30] Our data collection started with in-depth individual interviews using an inductive approach. Data analysis of the interviews revealed several stages and corresponding needs in decision-making, resulting in a preliminary decision-making framework. Next, a literature search was conducted to find comparable decision-making frameworks from earlier publications, to establish possible gaps in the preliminary framework and to spark new insights. Subsequently, research group meetings (co-authors AdM, WR, RR, MH and JH) were used to look at our preliminary framework from a bird's-eye view and to discuss these gaps in our framework, taking into account how the OFGs could be used to close these gaps. Finally, OFGs were carried out to determine whether women recognised their decision-making process in the presented stages and corresponding needs as described in the framework, and to gain insight into potentially inconclusive topics. Results from the OFGs were used to refine the framework, resulting in the final framework.

Study population and recruitment

The study population consisted of orthodox Protestant women aged between 18-40 years old. A purposeful sampling method was used. We explicitly selected participants aiming at a broad variety of women regarding pregnancy status, having children, age, membership to various orthodox Protestant church denominations, and residence in different regions of the Netherlands. Aim of this purposive sampling, as opposed to probability sampling, is to include 'information rich cases for indepth study'.[31] As we aimed to explore the decision-making process of women who were expected to make a decision about maternal pertussis vaccination in the near future, we recruited married women, knowing that becoming pregnant generally

is the wish of married couples of this religion. Key persons (individuals with close contacts within the orthodox Protestant community) provided entrance to the orthodox Protestant minority as this community is considered to be hard to reach. Key persons approached orthodox Protestant women to verify if they were willing to participate in the study, if so, the researchers would provide additional study information. Additionally, interviewed women were asked to approach other women from their network for participation in the study. This snowball sampling was used to reach women who could not be reached through key persons and to minimize selection bias by only including women of the key persons' networks. All interviewees were asked to participate in an OFG, as it was considered to be of added value if OFG participants had previously reflected on their decision-making process in an interview. Besides, other eligible participants were approached to participate in an OFG using purposeful sampling via key persons and through snowball sampling via interviewees and participants who already joined an OFG.

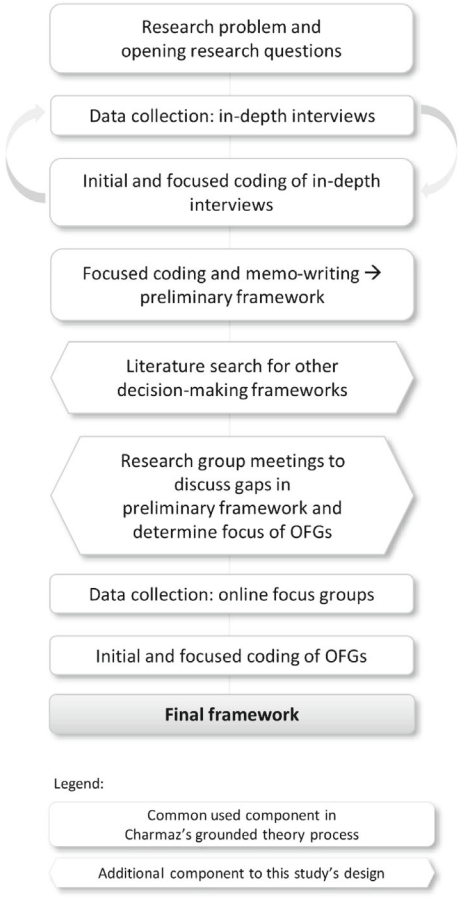

Figure 1. Flowchart of this study's constructivist grounded theory method

After an initial telephone contact with one of the researchers (AdM or DvN), interviewees and OFG participants were provided with written information about the study objective, interview or OFG procedure, and the voluntary nature of participation. After one week the researcher contacted the potential participant to answer any questions the participant might still have had. After oral consent, an interview appointment was made or participation in an OFG was scheduled. Written consent was obtained before the start of the interview or OFG. Participants received a gift voucher for participation.

Interviews

Semi-structured in-depth interviews were conducted between March and August 2017 by trained female interviewers (AdM, DvN and WR). The interviewers had knowledge of the orthodox Protestant community, yet were not members of an orthodox Protestant denomination. The interviews lasted 20-60 minutes, with a mean of 30 minutes. To create a confidential environment, interviews were held at the participants' homes. The interview started with an introduction to the study objectives. A topic guide, which contained several general open-ended questions about the needs for decision-making and the decision-making process, was used to preserve a basic structure in the interviews (see Table 1 for the English translation of the topic guide). The topic guide was developed by the authors and pretested in two pilot interviews; no adjustments were needed. If the participant was not familiar with the maternal pertussis vaccination, a short introduction was given on the subject (Table 1). Data were collected until data saturation was reached, after no new insights in the categories of the decision-making process or needs for decision-making emerged in the final interviews. Results from the interviews were used to shape the preliminary framework.

Literature search

Search terms used in PubMed were the MeSH terms "Vaccination" OR "Immunization" AND "Decision making", combined with "Framework" OR "Stage" OR "Model" OR "Phase" OR "Process" OR "Steps". The preliminary framework resulting from the interviews, and the frameworks following the literature search were discussed in research group meetings (with AdM, WR, RR, MH and JH), which resulted in a multistage decision-making framework, including needs for decision-making.

Table 1. Interview topic guide

Introduction: Familiarity with maternal pertussis vaccination
• Have you ever heard of the pertussis vaccination for pregnant women? If this is not the case, the interviewer provides the following introduction of the maternal pertussis vaccination: *The Health Council advises to provide a pertussis vaccination to every pregnant woman in the Netherlands. This vaccination will be given between weeks 28 and 32* of pregnancy. In response to the vaccination, the pregnant woman's immune system makes antibodies. These antibodies will be transferred to the fetus via the umbilical cord. Thus, the baby will be born with sufficient antibodies to protect him/her against pertussis during the first months of life.*
Decision-making process and needs
• How would you make the decision regarding getting this vaccination? • What do you need to make this decision? • Would you discuss this vaccination with others? Who would this be and what would you like to discuss?
Final decision
• What is the most important reason for you to accept or decline the vaccination? • Who makes the final decision?

** At the time of the interview and OFG data collection, the National Coordination Centre for Communicable Diseases Control of the National Institute for Public Health and the Environment advised pregnant women to receive the maternal pertussis vaccination between weeks 28 and 32 of pregnancy. In the current Dutch immunisation programme, pregnant women can receive the vaccination as from the twenty-second week of pregnancy.*

Online focus groups (OFGs)

In the final study phase, focus groups were carried out in an online environment, which allowed us to include women from different geographical areas in the Netherlands, as it offered the possibility of overcoming geographical distance among participants. Women could remain anonymous by participating under a nickname, which was considered an advantage as vaccination may be a sensitive topic for orthodox Protestants and anonymity could reduce social desirability bias.[18, 32] We used asynchronous OFGs, meaning that participants did not have to be online at the same time. Therefore, women had the ability to reflect on our questions, the responses of other women, and the response they wanted to share.[32]

In April and May 2018, three OFGs were conducted with a maximum of six participants per group. Before the start of each OFG, participants received written information about the maternal pertussis vaccination, instructions about the online forum, and a nickname and password. An OFG lasted from Monday to Friday, starting each morning with a 'question of the day'. (See Table 2 for the English translation of the online focus group topic guide). Women were asked to answer the researcher's questions and react to other participants' responses. During the day, the researcher (AdM) would post a second or third question in response to the group discussion. Results from the OFGs were used to refine the framework until consensus was reached.

Table 2. Online focus group topic guide

Monday	
Main Topic	Information
Introduction	You received information about the pertussis vaccination for pregnant women.
Questions	What was your first reaction? What did you like about the information? What did you dislike about the information? Could you make a decision based on this information?
Tuesday	
Main Topic	Health care professional and other people
Introduction	Imagine you are pregnant and your midwife offers you the vaccination.
Questions	How can your midwife support you in making a decision? Which support would you like to receive from another health care professional? Would you discuss the vaccination with someone other than the health care professional? And if so, who would this be?
Wednesday	
Main Topic	Deliberation: Religious beliefs
Questions	Do your religious beliefs play a role in your decision-making about the maternal pertussis vaccination? And if so, how are your religious beliefs involved in your decision-making?
Thursday	
Main Topic	Other deliberation themes
Introduction	Looking at your posts from past days, I noticed that you gather information, opinions and guidance in various ways, e.g. by searching The Internet, discussing with family or friends, praying, and reading in the Bible.
Questions	How do you weigh all this? Is it important for you to make a good decision? And do you know where this derives from? (only in OFG 2 and 3)
Friday	
Main Topic	Evaluation group meeting
Questions	How did you experience this online group discussion? Would an online forum or group meeting contribute to your decision-making? If there was a group meeting about the maternal pertussis vaccination in which information about the vaccination was shared and you could discuss the vaccination issue – would you go to such a meeting? Would it make any difference to you if this meeting was organised by a Christian organisation?

Data analysis

Interviews were recorded with a digital voice recorder and transcribed verbatim. To provide anonymity, references to individuals were removed from the transcripts. Transcripts were analysed using the qualitative software program ATLAS.ti 8. Two researchers (AdM, DvN) conducted the initial coding of the interview transcripts independently, in which lines and segments of the transcripts were coded line-by-line and solely based on the content of the data. Initial codes were reviewed, discussed and refined (AdM, DvN, WR) until consensus was reached. Using focused coding, codes were combined into categories (AdM, WR) including stages and needs in the

decision-making process. In the memo-writing process, these categories and codes were transformed into a preliminary framework.

After completion of the OFGs, all posted comments were adopted unchanged into the transcript. For the data analysis of the OFGs, two researchers (AdM, WR) analysed the OFG transcripts using initial and focused coding , taking into account that these codes and categories could differ from the interview codes and categories. Newly emerging codes and categories were discussed and refined until consensus was reached. Subsequently, emerging categories were compared with those in the preliminary framework, and used to adapt the framework.

This study adheres to the COREQ guidelines for reporting qualitative studies.[33] Quotes were translated from Dutch to English by the first and last author and then checked by an external bilingual reviewer.

Ethics and privacy

The Medical Ethics Committee (CMO) of the Arnhem-Nijmegen region assessed the study in February 2017 and concluded that it was exempt from their approval; reference no. 2017-3178.

Results

In total, 25 women participated in the study. Fifteen women participated in an individual interview and sixteen women took part in one of the three OFGs, of which six women had previously participated in an individual interview. Of the fifteen women participating in an individual interview, nine declined OFG participation, primarily because the OFG would be too time-consuming.

All participating women were married and most had children. Their children were either vaccinated, unvaccinated or partially vaccinated. Participant characteristics are shown in Table 3. Since the maternal pertussis vaccination was not yet implemented in the national immunisation programme at the time of the interviews and OFGs, participants were asked to hypothesize their future decision-making as if they were pregnant and had to decide on pertussis vaccination uptake.

Table 3. Participant characteristics of interviewees, interviewees who participated in an online focus group, and online focus group participants (n=25)

	Interviewees (n=9)	**Interviewees and OFG participants** (n=6)	**OFG participants** (n=10)
Years of Age (range)	23-36	24-37	26-36
Pregnancy status			
Pregnant	4	n/a	1
Not pregnant	5	1	9
Pregnant during interview or OFG	n/a	5	n/a
Children			
Yes	8	5	9
No	1	1	1
Children of participant are vaccinated			
Yes	4	2	5
No or not intended to	4	3	2
Partially*	0	1	2
Unknown or not applicable	1	0	1
Church denomination			
High level of conservatism	4	1	0
Moderate level of conservatism	4	3	9
Low level of conservatism	1	2	1

* Partially vaccinated= some of the participant's children were vaccinated and other children were not, and/or the participant's children had not received all recommended vaccinations. Abbreviations: OFG=online focus group; n/a = not applicable

Decision-making framework: stages and needs

A preliminary framework, which contained multiple stages and corresponding needs in the decision-making process, was constructed from the results of the individual interviews. After 15 interviews data saturation of the interviews was reached. The literature search resulted in three publications which visualized a vaccine decision-making framework: Bartolini et al. (2012), Brunson (2013), and McNeil et al. (2019).[34-36] The models of Bartolini et al. (2012) and Brunson (2013) included separate stages of decision-making, yet, only the framework of Bartolini et al. (2012) included needs for decision-making in these stages. The model of McNeil et al. (2019) described decision-making as a deliberative process. These frameworks were used in the research group meetings to refine our preliminary framework. Lastly, after the analysis of the OFGs, we stated that we gathered sufficient information in the three OFGs to complete the framework (Fig 2).

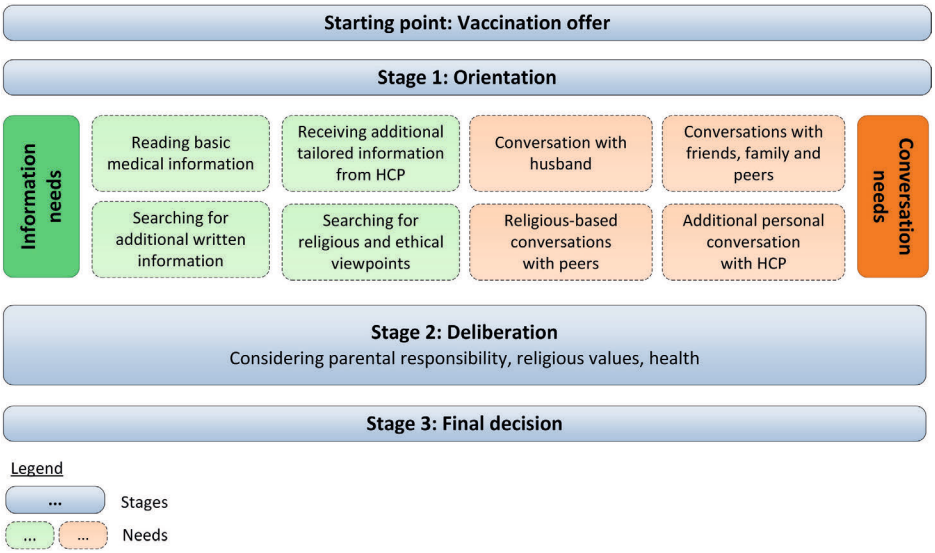

Figure 2. Framework of decision-making process on maternal pertussis vaccination among orthodox Protestant women

In the paragraphs below, the interview and OFG results are described collectively, following the structure of the stages and needs in the final framework, illustrated by quotes of participants (Table 4). The starting point of the framework is the Vaccination offer from the HCP, followed by three stages of decision-making. Stage 1 in the decision-making process is Orientation, in which women gather information and discuss the topic with others. In stage 2, Deliberation, women contemplate the values they consider to be most important in this vaccination issue. Stage 3 encompasses the Final decision to accept or decline vaccination. Women mentioned specific needs in the decision-making process most often in relation to their Orientation. These needs are categorised into Information needs and Conversation needs.

Table 4. Quotes from orthodox Protestant women during interviews and online focus groups

Stage 1. Orientation
Information need: Reading basic medical information
"A bit of information about the new [vaccine]. You can receive a vaccination during your pregnancy and then what? Why would you do that? So, certain motivations. [...] *I would very much like to know what consequences it has for the baby in my womb. Whether it has negative consequences as well, and if this is the case, I just want to know the truth.*" (Interview 8)
"If you have to make a decision based on this information (information provided prior to the OFG), *then you almost feel it is mandatory, because you don't have another choice. It is either vaccinating* (accepting the maternal pertussis vaccination) *or life-threatening* (if your newborn gets whooping cough)." (OFG1, woman 6)
Information need: Receiving additional tailored information from HCP
"If there are reasons to make the advice personal, I would like this information to be provided by the midwife, as well. I am thinking about certain (risk)factors which I might have and should, therefore, be discussed." (OFG1, woman 4)
She (midwife) *is very professional and knows a lot.* [...] *I consider her to be an expert, when it concerns babies.* (Interview 13)
Information need: Searching for additional written information
"Because I am used to view everything from different angles and to read more about it before I come to a consideration, I would also search for additional information. I would request and read the package insert. Based on this I would continue my search; there is various information from different perspectives to be found on The Internet." (OFG1, woman 5)
"The downside, I really find this a downside, because if you search on The Internet, which you actually shouldn't do, because you find a lot of, a lot of information which you cannot always assess to be reliable." (Interview 8).
"Now it is so explicitly pro, that if you also want to hear counterarguments, you must first research for this yourself." (OFG2, woman 9)
Information need: Searching for religious and ethical viewpoints
"You read the (orthodox Protestant) *newspaper, you read Terdege* (orthodox Protestant magazine), *you read, well, for example, this brochure from the NPV* (Dutch Christian patient organization) *that you receive."* (Interview 13)
"I would appreciate hearing about the ethical side. Especially in case of such a 'new' vaccination while the baby is still in the womb, I would really like to know more!" (OFG2, woman 16)
Conversation need: Conversation with husband
"We are on the same page about most things for that matter, fortunately. Yes, I think, I mean, you talk about it together. I think you search for information, or you read what you received somewhere. [...] *I would not look into this alone, no. It is really something you decide together."* (Interview 3)
Conversation need: Conversations with friends, family and peers
"I think I would mainly talk about it with others around me who are pregnant at that moment and who have to make the decision, or those who have just made the decision." (OFG2, woman 8)
"We, Christians, can think we know everything, but of course that doesn't have to be true. Sometimes you can learn, I think, from people who are not part of anything (people who are not religious) *and who decide on other grounds."* (Interview 5)
Conversation need: Religious-based conversations with peers
"It is, of course, also the case that people from the orthodox Protestant minorities most often rely on their own groups. [...] *Then you talk about it with your own people, maybe also because, yes, that is where you come from; it feels familiar and the choices they make, also feel good for you."* (Interview 7)

"I would be curious to know if others with the same religious beliefs would, for example, have ethical arguments on why to do it or why not. Sheerly for my own consideration." (OFG2, woman 14)
Conversation need: Additional personal conversation with HCP
"What I always like very much is, that it (information given by the HCP) *comes with empathy and a sympathetic ear and good arguments.* [...] *That means a lot to me."* (Interview 14)
"You don't expect information on principle issues from the midwife. [...] *I don't expect that such information can be compatible to our way of living and to our feelings and to our religious beliefs."* (Interview 11)
Stage 2. Deliberation
Parental responsibility
"In the end, I, myself, am responsible for the unborn child in the sense that I take care of my own body during pregnancy and in that way create circumstances that are as optimal as possible. I cannot impose that responsibility on someone else." (OFG1, woman 5)
"Actually, the feeling/maternal intuition is nearly the most important in making a decision." (OFG3, woman 15)
Religious values
"It is not the case that the Bible, which I read, says 'Thou shalt not vaccinate'. [...] *I really believe that God has given me intellect, which I shall have to use to make wise choices."* (Interview 12)
"That is the 'struggle' for us. We have our own responsibilities and we may use the available resources, but that doesn't mean that we blindly want to protect ourselves against everything (and, so, vaccinate). (OFG2, woman 9)
"In my opinion, you should make the decision in dependence on God, knowing that God is above all. However, you have your responsibility and you should use the available means (if ethically justified)."(OFG2, woman 12)
Health
"Then I would calculate the risks. [...] *Is the odds five thousand to one, or is the chance a hundred to one? Is the risk of a side-effect greater than its benefit? Or is the danger of not-vaccinating, for example, the chance that your child gets it* (pertussis)*, or that your child dies because of it* (pertussis)." (Interview 12)
"I try, with the resources available, healthy food and vitamins, to increase resistance. I'd do that rather than a vaccination. That is most important for me." (Interview 7)
Step 3. Final decision
"It remains our own responsibility if you do it or not (vaccinate) *and not because it is customary."* (OFG1, woman 1)
"In the end, it is not very relevant whether you do it or do not do it (vaccinate)*, but most of all that in your conscience you are certain that you did everything to receive the right information."* (OFG3, woman 15)

Abbreviations: OFG= online focus group; HCP= health care professional

Starting point of the decision-making process: Vaccination offer

Most women were unfamiliar with the maternal pertussis vaccination. One pregnant interviewee did not need an introduction of the vaccination, as she already had read some information about it. She could not recall the source (HCP or other) of the information. Women presumed that their midwife would notify them about the vaccination in one of their regular appointments during pregnancy. Some women, who refused childhood vaccinations on religious grounds, pointed out that they would

probably also refuse maternal vaccination. Nevertheless, they indicated that they would like to be informed about the vaccination offer and other possibilities to protect their unborn or newborn child against pertussis.

Stage 1 in the decision-making process: Orientation

Participants presumed that they would have many questions following the Vaccination offer. Therefore, women considered they would need time to gather and read information and discuss their options with others, to satisfy their Information and Conversation needs. Some women, especially those who expressed more hesitancy towards the vaccination, expected that they would orient themselves more broadly and extensively than others.

Information needs in stage 1 Orientation

Participants' initial information need was to receive basic information provided by HCPs. After which, women expected to manage the rest of their needs themselves; searching for information that they believed was relevant for them and discussing the vaccination issue with specific people in their surroundings.

Reading basic medical information. Women indicated they would first need basic, factual medical information that would answer their most pressing questions about pertussis and the vaccination, e.g. questions about vaccine safety and the necessity and effectiveness of the vaccine. Participants expected that this information would be provided in a brochure or website by the HCP or national public health service. They hoped that these brochures or websites would contain trustworthy, independent and non-directive information. However, mentioned by interviewees and supported by OFG participants, women expected the standard information would provide a one-sided viewpoint -one in favour of vaccination- and would contain insufficient information on which to base their decision.

Receiving additional tailored information from HCPs. Several participants wanted HCPs to tailor the information and/or motivation to vaccinate to their personal situation, e.g. if the participant had a medically complicated pregnancy or lived in a high- or low-risk area for pertussis incidence. Midwives were seen as the most trustworthy persons to provide this information. They were expected to have ample expertise about the topic and they would have the best interest for the unborn child and the pregnant woman in mind. Some participants thought that, in addition to their midwife, general practitioners (GPs), obstetrics clinic personnel and professionals from public health centres could also provide credible and solid information.

Searching for additional written information. Most participants indicated they would search for additional information on The Internet or in books. The Internet was assumed to create a complete information overview from different sources, however, some women stated they often found it difficult to make a selection of valid online information. Therefore, they would prefer a list of reliable, informative websites from HCPs. Websites of the national public health authority (RIVM) or midwife associations were thought to provide credible and essential medical information. Despite this, some women presumed that these websites might provide mainly positive aspects of the vaccination and, therefore, they would actively search for possible negative effects, and alternatives to vaccinations on websites from other sources, such as anti-vaccine movements and homeopathy practices.

Searching for religious and ethical viewpoints. To fulfil their needs for information on religious aspects of the vaccination, e.g., themes of divine providence, trust in God, and the responsibility of man, participants would seek for answers in the Bible and opinions written by representatives from their own religious constituency in books, on websites or in newspapers. Some women mentioned they highly valued the brochure from a Dutch Christian patient organisation, containing these main religious themes regarding vaccination. In addition, some women wanted to read more about the medical ethical view on the vaccination to determine its proportionate use in the prevention of illness, especially since the vaccination could influence the natural process of pregnancy given by God.

Conversation needs in stage 1 Orientation

Most participants felt the need to discuss the vaccination with others; their husband, friends, family, peers, neighbours, and acquaintances. In these conversations, they assembled opinions, information, and experiences about the vaccination issue.

Conversation with husband. Participants considered their husband to be the most important person to discuss the vaccination issue with since husband and wife should decide about the vaccination together. A few women would only discuss this vaccination issue with their husband, as they considered this decision to be a personal matter. Some couples would read medical and religious information together and/or pray together for God's support in their decision-making.

Conversations with family, friends and peers. Conversation partners preferred by the participants, besides the husband, were women who stand close to them, who have to make the same decision or have an equal opinion about vaccinations. Several women pointed out that having a conversation with someone who has a contrasting opinion about vaccinations, or one who has a different religious background or no religious

background at all, could create a more complete view about the matter. Face-to-face conversations were more often experienced as meaningful conversations, compared to online conversations. Most women thought that sharing their doubts, opinions and/or considerations in a group meeting would have an added value in their decision-making.

Religious-based conversations with peers. Discussions about religious and ethical topics were confined to one-on-one or group conversations with other orthodox Protestants or Protestant Christians. The aim of these conversations was to gather religious and/or ethical viewpoints or to serve as confirmation of one's own opinion. Some women thought that group meetings about the maternal pertussis vaccination provided by a Christian organisation would give a more objective and nuanced (ethical) view on the vaccination, and these meetings were expected to be more considerate of their religious beliefs than a group meeting provided by the midwife practice.

Additional personal conversation with HCP. Several participants felt the need for an open, personal consultation with their HCP, which was not (primarily) based on receiving factual medical information. These women reckoned they would like to hear the HCP's personal experiences with pertussis and/or personal viewpoints on the vaccination. However, both women who did and did not prefer a personal consultation with their HCP, disliked it when HCPs imposed their opinion on them following their strong desire to make a personal decision. In addition, HCPs were not expected to discuss religious views on the vaccination, since religious considerations are seen as a personal matter.

Stage 2 in the decision-making process: Deliberation

Participants mentioned an overall need for a timeout moment during the decision-making process to contemplate the information and viewpoints they gathered in their Orientation stage, and the personal values they considered to be most important in their decision concerning this vaccination issue. In this Deliberation stage three themes of combined values could be identified: parental responsibility, religious values and health. Often various personal values coexisted in this Deliberation. However, some participants indicated that one main value could outweigh other values. For instance, many highly conservative orthodox Protestant participants mentioned they considered their trust in God (religious value) to be most important and, therefore, they might choose not to vaccinate. This could outweigh their understanding that the vaccination can prevent a pertussis infection (health).

The findings did not indicate separate needs for decision-making in the Deliberation stage.

Parental responsibility

Most participants experienced a strong sense that, as parents, they are responsible for their child's health, a responsibility that could not be entrusted to others. Particularly pregnant women and firsttime mothers mentioned they considered it to be their primary role as an (expectant) mother to ensure a healthy pregnancy and protect their (unborn) child against all negative influences, if possible. A few experienced mothers presumed that they would choose to accept or decline vaccination based on their intuition, which would give them the feeling of 'doing the right thing' as a parent. Some women indicated they wanted to be able to explain their well-considered decision to their child in the future.

Religious values

The religious values regarding this vaccination topic could be divided in two main issues. On one hand, the issue of interfering with divine providence and absolute trust in God, including his plan regarding sickness and health. For some participants, accepting vaccination implied distrust in God's protection and the life that is predetermined for them. In addition, some women considered vaccination an undesirable intervention in light of 'human enhancement' i.e. that mankind tries to outdo God.

On the other hand, women referred to the issue that God has given mankind the responsibility to use available knowledge to make a well-considered decision. Some women considered the vaccination a gift from God, as mankind was given the capability to develop vaccines to keep children healthy. Several participants expressed that they experienced a strong conflict between these religious values.

Ultimately, it was considered to be most important that a decision was made in line with one's own religious beliefs, and one's personal relationship with God.

Health

Participants would use the gathered information to weigh all health-related pros, cons, and alternatives to the vaccination which they considered relevant for their personal situation. Participants frequently mentioned that they aimed to strike a balance between their perceived risk and severity of pertussis, and their perceived benefit of the vaccine. The possible risks of the vaccines were mostly discussed in relation to the unknown negative influence it may have on the pregnancy and the unborn child. However, some participants stated that it was better if she, a healthy

adult, would receive the vaccine, instead of their vulnerable newborn child. In contrast to women who tended to accept vaccination, hesitant women highly valued the alternatives to the vaccination. More hesitant participants emphasised the added value of preventing pertussis infection by breastfeeding your baby, healthy nutrition, and taking homeopathic products.

Stage 3 in the decision-making process: Final decision

Even though this study was based on a hypothetical situation and women had not yet made a final decision, several participants mentioned their intention to either accept or decline this vaccination during pregnancy. Most women wanted to make a well-considered decision and indicated that, if they were given enough time for Orientation and Deliberation, they would be able to do so. A few women who objected to vaccinations on religious grounds expected their decision-making process to be concise, resulting in refusing the maternal pertussis vaccination. Overall, all women considered it to be of great importance that husband and wife would make the final decision together.

Discussion

In this study, we distinguished stages and needs in the decision-making process regarding the newly introduced maternal pertussis vaccination in a vaccine-hesitant religious population. The framework, resulting from the findings in this study, describes the decision-making process and included an Orientation stage, a value-based Deliberation stage, and Final decision stage. The needs for decision-making are concentrated in the Orientation stage and are categorised into Information needs and Conversation needs.

In contrast to our study, conducted in a religious group in an European country, the studies on the decision-making process found in the literature search were carried out among general populations in North and South America.[34-36] The religious background of the participants and/or the influence of religion on the decision-making process within these studies was unknown. Nevertheless, in the frameworks and descriptions of the decision-making process provided in these publications, we found striking similarities in the processes of decision-making compared to the decision-making process of our study population.[34-36] Resembling results were also found in other publications, which did not contain a decision-making framework or model, yet, which did describe comparable elements in the decision-making process, as discussed below.[26, 37-55] This implicates that, even though our study is conducted among a vaccine-hesitant religious group in the Netherlands, our framework could be applicable to a broader population.

The desire of parents to actively orient themselves on the vaccination issue by fulfilling both information and conversation needs was broadly supported by other studies on vaccine decision-making.[25, 34, 35, 37, 44, 52] In our study, vaccine hesitant religious women were inclined to follow a thorough Orientation stage by actively searching for information and having conversations with others. Like Brunson's 'searchers', they conduct their own research by seeking information from multiple pro- and contra-vaccination published sources and tend to be critical about the information they obtain.[35] Or like Wiley's 'proactive types' they actively search for information and use their HCP as an information source.[52] Consistent with our results, HCPs are considered to be trustworthy information sources.[37, 47] Yet, compared to vaccine-acceptant parents, vaccine-hesitant parents are more critical about which information source or HCP they trust.[37, 48] In addition, most women value conversations about the vaccination issue with others, such as friends, family and peers, which was also the case in our study.[25, 26, 34, 44, 51, 52] Research among social networks indicates that vaccine-hesitant parents include more persons in their social networks related to their decision-making than vaccine-acceptant parents.[42]

Before they would make a decision, participants wanted to deliberate over the vaccination issue, guided by personal values they considered to be most important. This study supports evidence from previous findings, showing that vaccine-hesitant parents follow a more thorough deliberation process by carefully weighing the pros, cons, alternatives and consequences of accepting or refusing vaccination, compared to acceptors.[36, 49] There is a relatively small body of literature that emphasizes the deliberation of values in regard to vaccination decision-making.[38, 40, 53, 56]

Similar to the orthodox Protestant participants, parents in other studies valued the importance of 'being a good parent' by taking responsibility for their child's health in the context of childhood vaccinations as well.[17, 39, 46, 54] Corresponding to our results, these findings state that taking parental responsibility can result in accepting vaccination to protect a child from disease, or decline vaccination to protect a child from harm caused by the vaccine. Considering the observed critical and proactive attitude of the orthodox Protestant women in this vaccine decision-making process, it is noteworthy that the present generation of orthodox Protestant women follows the rising trend of self-determined parents who want to take responsibility for their child's health and take a proactive role in their decision-making processes which is seen in many high-income countries.[23, 41, 44, 45] The gendered aspect found in others studies, that women are often the primary decision-makers, was not recognized by our respondents, as they stated that the final vaccine decision-making is done by husband and wife together.[44, 55]

As religion plays a central role in the lives of orthodox Protestant women, religious values influenced their vaccination decision and health attitudes in general, which has previously been found in this religious group, as well as in other groups with a religious or spiritual lifestyle.[18, 50, 57]

According to some participants in our study, a healthy lifestyle and nutrition could prevent one's child from disease and, thus, serve as alternatives to vaccinations. Similar health values have been mentioned in relation to vaccination decisions by parents with an anthroposophical lifestyle.[17, 39, 43] The correspondence of our and other findings on the influence of personal values on decision-making and acceptance on vaccination, can indicate that overall, similar to our participants, parents feel a need for value deliberation to make a well-considered decision regarding vaccination.

Earlier research indicates that the involvement of HCPs and religious leaders in the vaccine decision-making process of orthodox Protestant parents, besides providing and explaining medical information (HCP) or biblical principles (religious leaders), is limited.[58, 59] A study among Dutch HCPs indicated that whether or not a HCP discussed vaccine decision-making with orthodox Protestant parents depended on the willingness of these parents to engage in such a discussion and on the personal characteristics and communication skills of the HCP.[59] As HCPs' communication skills and content knowledge are of great importance to address vaccine hesitancy, this framework can provide HCPs with adequate insight to guide parents who ask advice from this HCP.[60] Further, health policies and finances should be organized as such, that HCPs supporting these parents, have sufficient time, resources and opportunities to strengthen their vaccination consultations.[60, 61]

Strengths and limitations

To establish a vaccine decision-making framework we used an explorative multimethod approach, combining in-depth interviews and OFGs for data collection with a literature search and research group meetings, to establish possible gaps and refine our preliminary framework. The data-triangulation of interviews and OFGs in combination with the literature search and research group meetings made it possible to first explore the individual decision-making process and, subsequently, gain deeper insight into the presented stages and corresponding needs of decision-making that were shared in a group setting. The group discussions emphasized which needs and opinions were widely supported and which were more individually-based. Additionally, it is expected that the anonymous participation and the possibility for women to respond in their own pace, contributed to the reliability and completeness of the OFG findings. Data validity was further increased by using environmental

triangulation, as the interviews were conducted at the participants' homes and the focus groups in an anonymous online environment.

With regard to limitations, our purposeful sampling resulted in a small, yet, varied study sample of church denomination, age, pregnancy status, vaccination status, and number of children in participants. Data saturation was reached. Due to the small study sample, however, results have to be interpreted with caution. Still, the results give a valuable glimpse into understanding the decision-making process and its related needs in this vaccine-hesitant group. Participants' education level was not included in our data gathering. It is possible that more higher than lower educated women participated in our study, more highly educated woman in various studies show an intense need for information seeking and reasoned decision-making, similar to the women in our study.[41, 45, 62] On the other hand, other sources indicate that this thorough decision-making process may also characterize (orthodox) Protestants in general.[18, 63] Nevertheless, we recommend future vaccination studies to investigate the influence of education level on decision-making, as well.

Finally, the timing of the data collection was considered to be both a strength and a limitation of the study. This study was conducted before the implementation of the maternal pertussis vaccination in the Netherlands. Therefore, we were able to explore women's needs for decision-making before their needs were affected by the national immunisation campaign and standardised procedures and interventions. Conducting this study on a hypothetical situation allowed women to be more honest and open about their decision-making without feeling additional social desirability effects. The drawback of this time point of investigation, however, is that women had to hypothesize how they would conduct their decision-making process in the future, which some women found challenging. Future research is required to confirm our findings in a real decision-making situation.

Conclusion

Our results indicate that, after the Vaccination offer of the maternal pertussis vaccination, Dutch orthodox Protestant women gather information and discuss the vaccination issue with others to orient themselves on the vaccination. Subsequently, the study results imply that women deliberate over the values they consider to be most important in this vaccination decision –parental responsibility, religious values and/or health- to make a well-considered Final decision.

Our framework provides a glimpse into the decision-making process of vaccine-hesitant religious women and can be used to assist HCPs. Alongside providing and

explaining information, HCPs could support women, who experience difficulties in vaccine decision-making, by providing additional consultations and adjust their communication to the stages and expressed needs in our framework. Therefore, policymakers and public health institutes should provide HCPs with means and opportunities to meet women's decision-making needs. Future research that builds upon the results of this study's findings, accompanied by experiences in clinical practice, can be used to determine in which manner HCPs and other professionals can facilitate women in their different vaccine decision-making stages. As our decision-making framework describes a decision-making process that could be similar to the process of other vaccine-hesitant subgroups, future studies should investigate whether the stages of decision-making in our framework can be found in other vaccine-hesitant subgroups as well.

Declarations

Acknowledgments

We wish to thank the participants for sharing their thoughts and experiences. This study would not have been possible without the help of key persons to recruit study participants, with special thanks to Henri Spaan and Pieternel Spaan-van Braak. We want to thank Merthe Broekman-Mulder for her contribution to the translation of the quotes and topic guides, and review of the manuscript.

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Data Availability
Participants have given their informed consent for the use of anonymized fragments of qualitative data. Participants did not consent to provision of the full raw dataset to persons other than the research team. Since the raw interviews and transcripts contain sensitive information and study participants are part of a close-knit community, even anonymized raw data can seriously compromise their confidentiality. Therefore, current Dutch privacy law and institutional regulations prevent the a priori sharing of the full raw dataset. Considering the importance of data-sharing and providing insight into the research, data access will be considered upon request, evaluating each inquiry individually. Requests for data access may be sent to the medical ethical committee of the Radboud University, who can be contacted at commissiemensgebondenonderzoek@radboudumc.nl.

Funding
This research study was supported by the research fund of the Dutch National Institute for Public Health and the Environment (RIVM), the Netherlands, for local Public Health Services. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Conflict of Interest
The authors have declared that no competing interests exist.

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Supplementary materials

File S1. Topic guide interviews in Dutch (PDF). Not included in this thesis. Available online at https://doi.org/10.1371/journal.pone.0242261.s001

File S2. Topic guide online focus groups in Dutch (PDF). Not included in this thesis. Available online at https://doi.org/10.1371/journal.pone.0242261.s002

Chapter 6

Deciding about maternal pertussis vaccination: association between intention, and needs and values in a vaccine-hesitant religious group

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Vaccine, 2022;40: 5213-5222

Abstract

Introduction

This study investigated the decision-making process with regard to maternal pertussis vaccination (MPV) among Dutch orthodox Protestant women. We used a framework describing three stages of decision-making: an orientation stage -outlining women's neefds to receive information and to conversate with others-, a deliberation stage -outlining women's personal values for contemplation-, and a final decision stage.

Methods

A cross-sectional survey was conducted prior to the introduction of MPV in the Dutch National Immunisation Programme. Univariate multinomial logistic regression analysis was applied to determine the association between intention to accept MPV and women's information needs, conversation needs, and needs concerning health care providers (HCP). Using factor analysis, deliberation domains were identified from the value-based statements. Multivariate multinomial logistic regression analysis was used to determine the association between intention and the deliberation domains.

Results

In total, 467 questionnaires were included. If being offered the MPV, the majority of the women (56%) would be undecided about accepting MPV (undecided women), 32% would certainly refuse (refusers), and 12% would certainly accept the MPV (acceptors). Acceptors and undecided women showed the highest information needs and needs concerning HCPs, undecided women showed the highest conversation needs, and refusers showed the highest needs to read vaccine-critical information and information from alternative (non-governmental) health sources. Three deliberation domains were identified: *trust in the vaccine and vaccine-providing authorities*, *individual deliberate decision-making* and *contemplating religious arguments*. Acceptors scored highest on the deliberation domain *trust in the vaccine and vaccine-providing authorities*. Undecided women showed a higher score on *individual deliberate decision-making* than refuser.

Conclusion

The differences and similarities we found among acceptors, undecided women, and refusers in the orientation and deliberation stage of orthodox Protestant women provide relevant insights for HCPs and vaccine policy makers, that can be used in the development and enrichment of tailored vaccination information and consultation.

Key words: Decision making; Intention; Vaccine hesitancy; Health Personnel; Values; Religious beliefs

Introduction

In 2019, WHO ranked vaccine hesitancy as one of the top ten global health threats. Vaccine hesitancy, defined by the SAGE Working Group as "the reluctance or refusal to vaccinate despite the availability of vaccines", has made it more difficult to maintain high vaccination coverages in many high-income countries.[1] Outbreaks of vaccine-preventable infectious diseases often originate in geographically and socially clustered communities with lower vaccination coverages, for example in vaccine-hesitant ethnic and religious minorities.[2-5]

Although maternal pertussis vaccination (MPV) is provided free of charge, in several countries the vaccination uptake remains relatively low, e.g. 43.6% in New Zealand, 49.9% in Ireland, 64.0% in Victoria (Australia), ~65% in England, and 69.3% in Belgium.[6-10] In the Netherlands, MPV vaccination coverage is estimated at 70%.[11] Vaccine hesitancy is known to be of influence on MPV decision-making, which may partially explain the lower uptake among pregnant women.[12, 13]

To address women's hesitancy to accept MPV, it is important to understand their decision-making process with regard to MPV; that is, the personal cognitive process preceding one's final decision to accept or refuse vaccination. Outlining this decision-making process is complex. It is influenced by factors on the individual (e.g., knowledge and values), interpersonal (e.g., friends and family), organisational (e.g. recommendation of health care professionals), community (e.g. sociocultural perspective on vaccinations), and public policy level.[14, 15] Searching for and reading information about the vaccination; discussing the vaccination with others; and deliberating over the vaccination are often part of parents vaccine decision-making process.[16-19]

The orthodox Protestant community in the Netherlands is historically characterized as vaccine-hesitant subgroup. In the Netherlands, about 250,000 people are member of an orthodox Protestant church (~1.5% of the Dutch population). The mean vaccination coverage of childhood vaccinations among orthodox Protestants is ~60%.[20-22] Orthodox Protestant denominations can be classified in clusters based on their level of conservatism and vaccination coverage: clusters with vaccination coverage <25% (high level of conservatism), vaccination coverage 50-75% (moderate level of conservatism), and vaccination coverage of >85% (low level of conservatism).[20] In addition to higher conservatism, lower levels of education, and parents not being vaccinated themselves are associated with lower vaccine uptake among parents concerning vaccinations for their children.[22] Orthodox Protestants highly value their belief in the Bible and their biblically confessions. Their health behaviours and

health decision-making, including vaccination decisions, are strongly influenced by their religious beliefs. Orthodox Protestants value well-considered decision-making in line with their personal religious beliefs.[23, 24] A qualitative study among orthodox Protestant parents found that religious arguments in vaccine decision-making were based on religious doctrine, their trust and personal relationship with God, and/or the belief that vaccination is a gift from God to be used in gratitude.[25]

In a recent qualitative study, we visualised the MPV decision-making process and related needs for decision-making among orthodox Protestant women in a framework (see Fig. 1).[23] The framework contains three stages of decision-making: an orientation stage, a deliberation stage, and a final decision stage. The orientation stage outlines women's needs to receive information and to conversate with others about the MPV, including their health care providers (HCP). The deliberation stage reflects the stage in which women want to contemplate personal values concerning the MPV. In the final decision stage, women reach their decision to accept or refuse MPV. Based on their desire for well-considered decision-making, most orthodox Protestant women will follow the orientation and deliberation stage with the comprehensiveness of the decision-making process varying among women.[23] Other than models focused on behavioural change, our framework conceptualizes decision-making. However, the orientation and deliberation stage in our framework combined, show similarities with decision-making stages in behavioural models, such as The Transtheoretical Model (Prochaska), the Precaution Adoption Process Model, and the Rubicon model. [26-28] Nevertheless, our framework solely focuses on describing how individuals come to an informed, deliberate decision and is not formulated from the perspective of HCPs or policy-makers with a focus on the cognitive and motivational process towards behaviour change (e.g. vaccination acceptance). Based on the findings in the qualitative study [23], we hypothesized that all women follow the orientation and deliberation stage, irrespective of whether they are intended to accept or refuse vaccination, or are still undecided. Yet, we think that women's needs in the orientation stage and their value contemplation in the deliberation stage differ among women who intend to accept vaccination, or refuse vaccination, or are still undecided.

To be able to respond better to women's needs and concerns in the MPV decision-making process, it is important for HCPs to gain knowledge and understanding of the needs and values that are important for this decision. The first purpose of this study was to quantify orthodox Protestant women's information needs, conversation needs, and needs concerning HCPs in the orientation stage of the MPV decision-making process and to determine the association between women's intention to vaccinate and their decision-making needs. The second objective was to explore the association between women's values and intention to accept MPV.

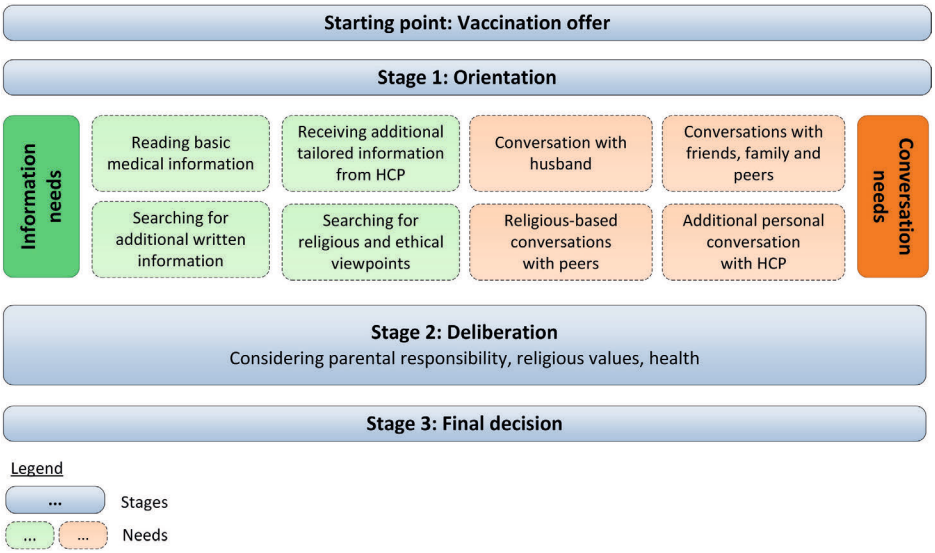

Figure 1. Framework of the maternal pertussis vaccination decision-making process among orthodox Protestant women (figure originally published in Plos One) [23]

Methods

Study population and sampling

A cross-sectional survey was conducted in October 2018-January 2019, prior to the introduction of the maternal pertussis vaccination (MPV) in the Dutch national immunisation programme (NIP) in December 2019.[29] Women between 18 and 40 years of age with an orthodox Protestant background were asked to participate in the study. Orthodox Protestant background was based on membership to an orthodox Protestant church that in the recent past or present expressed religious objections to vaccination.[22]

About 75% of the orthodox Protestants live geographically clustered in the so-called Dutch Bible belt, i.e. orthodox Protestant municipalities.[21, 30] Orthodox Protestant municipalities are often defined as municipalities with ≥5% votes for the orthodox Protestant political party, the Staatkundig Gereformeerde Partij (SGP).[21]

For this study, orthodox Protestant participants were recruited through a selection of midwife and obstetrical practices, and child health clinics situated in orthodox Protestant municipalities, orthodox Protestant social media and websites of orthodox Protestant online communities, an orthodox Protestant newspaper, an orthodox Protestant university of applied science, and key persons (individuals with close contacts in the orthodox Protestant community). Means of communication for

recruiting participants were flyers, posters, and online banners referring women to the study's website. In addition, the online community 'Refoweb' and the university of applied science approached women by using invitation emails. Moreover, snowball sampling was used by asking participating women to invite orthodox Protestant female friends and family members for participating in the study.

Questionnaire

The content part of the questionnaire contained questions about intention, information needs, conversation needs, needs concerning HCPs, and value-based statements. Prior to answering these questions, participants received some key information on MPV. In answering the questions, participants were asked to imagine being pregnant and being offered the MPV.

Women could indicate their intention to accept MPV by answering the question "Would you want to receive the MPV during pregnancy?" with: 'no, certainly not', 'probably not', 'probably' and 'yes, certainly'. Questionnaire items on needs and values in the questionnaire were based on our previous qualitative study among orthodox Protestant women in which we explored their MPV decision-making process. [23] Questions on information needs included whether participants wanted to receive or search for information, and the desired content and source of this information. Conversation needs contained questions about if and with whom participants would like to talk about the MPV. Needs concerning HCPs included the need to receive an explanation about the pros and cons or personal advice about the MPV from the midwife or child health clinic physician. Additionally, the questionnaire included 14 value-based statements to which women could respond their level of (dis)agreement on a six-point Likert scale from 'totally disagree' to 'totally agree'.

Assessed sociodemographic characteristics were age, education level, church denomination, living in an orthodox Protestant municipality (≥5% votes for the SGP) or not (<5% votes for the SGP), relationship status, number of children, pregnancy status, participant's childhood vaccination status, partner's childhood vaccination status, children's vaccination status (women with children), future children's vaccination intention (women without children), and personal experience with pertussis. Women who were pregnant and/or gave birth in the two years prior to answering the questionnaire were asked if they had received a pertussis vaccination during pregnancy (available at that time at own request and expense).

The questionnaire (English and the original Dutch version) is included in the supplementary material (Appendix 1. Questionnaire; Appendix 2. Questionnaire in Dutch).

Statistical analysis

Data were analysed using IBM SPSS Statistics 25. Participants who did not reach the final page or answered less than 80% of the crucial questions on needs, value-based statements, and/or sociodemographic variables were excluded from analysis.

In the data analysis, three categories of intention to accept MPV were used: 'will certainly accept MPV' (acceptors) (=0), 'undecided about accepting MPV'; women who would probably accept or probably refuse MPV (undecided women) (=1), and 'will certainly refuse MPV' (refusers) (=2). Following a descriptive analysis of the sample (frequencies and percentages), univariate multinomial logistic regression analysis was used to determine the crude odds ratio (COR) between intention to accept MPV and women's decision-making needs.

A principal axis factor analysis was conducted on the 14 value-based statements with oblique rotation (direct oblimin) to identify deliberation domains (Appendix 3. Data analysis factor analysis and deliberation domain calculation). For the factor analysis, cases with missing values in the value-based statements were excluded listwise. Univariate multinomial logistic regression analysis was used to determine the crude odds ratio (COR) between intention to accept MPV and each deliberation domain. Subsequently, we calculated the adjusted odds ratios (AORs) between intention to accept MPV as outcome variable and the mean values of the deliberation domains as predictor variables, corrected for possible confounders (i.e., sociodemographic variables that were significantly associated with intention in the univariate multinomial logistic regression models). We did not include the needs for decision-making in the multivariable model, as we aimed to identify which needs were part of the orientation stage amongst participating women rather than identifying their relative importance at the group level. As deliberation domains are continuous variables, the AORs represents the increase in odds that women are acceptor, rather than refuser, or undecided woman rather than acceptor/refuser, as a the mean value of the deliberation domains increases with one unit (one-unit increase). For complete case analysis missing values were deleted listwise. For all analyses, the significance level was set at $p<.05$.

The Medical Ethics Committee (CMO) of the Arnhem-Nijmegen region assessed the study and concluded that it was exempt from their approval; reference no. 2018-4680. Questionnaires were completed anonymously.

Results

A total of 765 woman started the questionnaire. Of these participants, 480 reached the final page and completed more than 80% of the questionnaire. After excluding 13 participants without an orthodox protestant background, a total of 467 questionnaires were included for analysis (Fig 2).

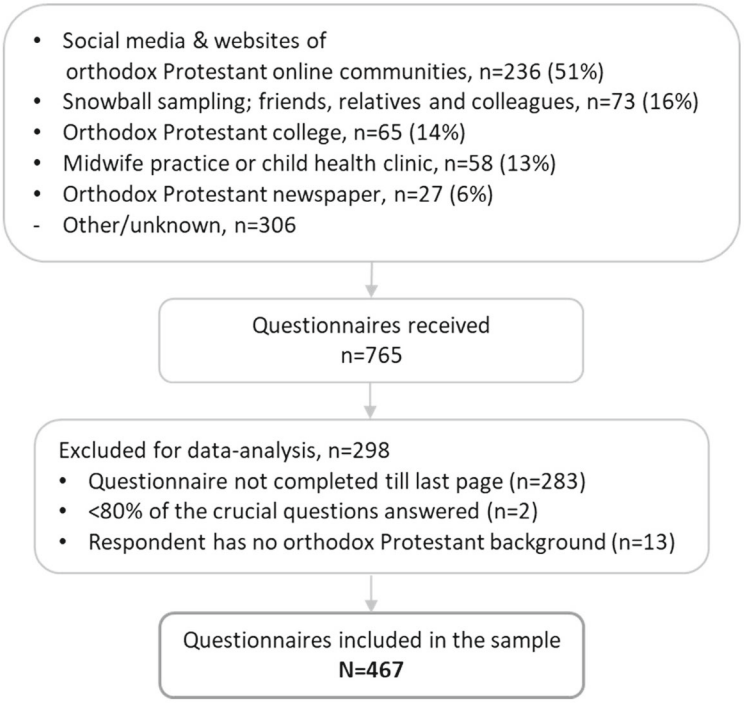

Figure 2. Flowchart of respondent selection

Participants' age was fairly equally divided over the age groups (Table 1). Most participants had an intermediate (52%) or high (44%) education level. Almost half of the respondents were member of a moderately conservative church denomination and almost three-quarter of the sample lived in orthodox Protestant municipalities. The majority of the women had a partner (83%) and on or more children (61%). One hundred women were pregnant (21%). Of the participants, partners, and children, respectively 36%, 34% and 29% did not receive childhood vaccinations. Of the participants without children, 28% intended to refuse all vaccinations for their children.

Table 1. Sociodemographic and vaccination-related characteristics of orthodox-protestant women in the Netherlands (N=467)

Sociodemographic factors	n (%)
Age, in years, n=467	
18-22	105 (22.5%)
23-28	140 (30.0%)
29-34	136 (29.1%)
35-40	86 (18.4%)
Educational level, n=467	
Low education level [x]	23 (4.9%)
Intermediate education level [+]	241 (51.6%)
High education level [#]	203 (43.5%)
Church denomination, n=467	
High level of conservatism [a]	67 (14.3%)
Moderate level of conservatism [b]	224 (48.0%)
Low level of conservatism [c]	91 (19.5%)
Protestants with orthodox Protestant affinity [d]	85 (18.2%)
Living in an orthodox Protestant municipality, n=454	
Yes living in a municipality with ≥5% votes for SGP*	327 (72.0%)
Relationship status, n=467	
Has a partner	387 (82.9%)
Children, n=467	
No children	184 (39.4%)
1 child	74 (15.8%)
2 children	95 (20.3%)
3 children	62 (13.3%)
4 or more	52 (11.1%)
Pregnancy status, n=467	
Pregnant	99 (21.2%)
Not pregnant	341 (73.0%)
Possibly pregnant /unknown	27 (5.8%)
Childhood vaccination status of the participant, n=461	
Completely vaccinated	264 (57.3%)
Partially vaccinated	31 (6.7%)
Not vaccinated	166 (36.0%)
Childhood vaccination status of partner, n=364	
Completely vaccinated	205 (56.3%)
Partially vaccinated	37 (10.2%)
Not vaccinated	122 (33.5%)

Table 1. Sociodemographic and vaccination-related characteristics of orthodox-protestant women in the Netherlands (N=467) (continued)

Sociodemographic factors	n (%)
Vaccination status of child(ren), n=280	
Completely vaccinated	157 (56.1%)
Partially vaccinated	43 (15.4%)
Not vaccinated	80 (28.6%)
Vaccination intention for future children, n=143	
Intended to accept all childhood vaccination	66 (46.2%)
Intended to accept some childhood vaccinations	37 (25.9%)
Intended to accept no childhood vaccination	40 (28.0%)
Participant had pertussis herself, n=467	
Yes	84 (18.0%)
Child(ren) had pertussis, n=467	
Yes	34 (7.3%)
Participant knew close contact with pertussis, n=467	
Yes	165 (35.3%)
Participant is vaccinated against pertussis during pregnancy in the past, n=252	
Yes	11 (4.4%)
Intention to accept maternal pertussis vaccination, n=414	
Will certainly accept MPV	51 (12.3%)
Undecided about accepting MPV	231 (55.8%)
Will certainly refuse MPV	132 (31.9%)

Abbreviations: SGP= Staatkundig Gereformeerde Partij (Reformed Political Party), MPV=maternal pertussis vaccination.

[x] No, primary, prevocational, intermediate secondary or lower vocational, or lower professional education

[+] Intermediate vocational education, higher secondary education or pre-university education

[#] Higher professional education or scientific education

[a] Reformed Congregations in the Netherlands (GGiN), Old Reformed Congregations (OGG)

[b] Reformed Congregations (GG) or Restored Reformed Church (HHK)

[c] Christian Reformed Churches (CGK) or Reformed Bond (within Protestant Church in the Netherlands)

[d] Protestant Church in the Netherlands (PKN), former member of the above mentioned orthodox Protestant church denominations, or other protestant church denomination

* Voting proportion for the SGP in the Dutch National Elections for seats in the House of Representatives in 2017

Table 2 shows the associations between intention to accept MPV and decision-making needs in the orientation stage of the MPV decision-making framework. If being offered the MPV during pregnancy, the majority of the women would be undecided about accepting MPV (56%), 32% would certainly refuse (refusers) and 12% would certainly accept the MPV (acceptors) (Table 1). The proportion of undecided

women was higher among women without children (61%, 101/166), than women with children (52%, 130/248).

Across all three intention groups, most participants would like to receive information about MPV during pregnancy (73%) and would search for information on the Internet (68%) (Supplementary material; Table S1). Most favoured information topics among women who expressed information needs were: possible negative influences of the vaccination for the baby (92%), the severity of pertussis (80%), and possible negative side effects of the vaccination for pregnant women (80%).

Conversation needs showed that the large majority would discuss the vaccination with their partner (86%) and would talk about the vaccination with others (87%). Favoured conversation partners were female friends (65%), sisters (46%), and parents (46%) (Supplementary material; Table S1). Regarding the needs concerning HCPs, most women preferred gaining information and advice from the midwife over the physician of the child health clinic; and an explanation about the pros and cons of the vaccination over personal advice (Supplementary materials; Table S1).

Univariate multinomial logistic regression analyses showed differences and similarities in information needs, conversation needs and needs concerning HCPs among acceptors, undecided women, and refusers (Table 2). Both acceptors and undecided women showed a statistically significantly higher need to receive written information, to search for information on the Internet, to visit the website of the National institute for Public Health and the Environment (RIVM), to join a group meeting, to receive an explanation about the pros and cons of the MPV from a midwife or child health clinic physician, or to receive personal advice from a midwife or child health clinic physician, compared to refusers.

Undecided women indicated to have a significantly higher need to hear or read experiences of other women about their MPV decision, to discuss the vaccination with their partner using the collected information, and to conversate with other people about MPV, compared to both acceptors and refusers.

Refusers were found to have the highest need to visit a vaccine-critical website (Dutch Association for Critical Vaccination (NVKP) and/or Vaccine Free Foundation), compared to acceptors and undecided women. The need to hear or read information from homeopathic or natural medicine health vision, was highest among refusers, followed by undecided women.

Table 2. Univariate multinomial logistic regression models: association of intention to accept maternal pertussis vaccination with needs from the orientation stage among orthodox Protestant women (N=414)

	Intention to accept maternal pertussis vaccination (MPV) [a]				MLR Acceptors vs. refusers COR (95%CI)	MLR Undecided women vs. acceptors COR (95%CI)	MLR Undecided women vs. refusers COR (95%CI)
	Acceptors, % (n)	**Undecided women**, % (n)	**Refusers**, % (n)	n			
Information needs							
Would you like to receive information about MPV during pregnancy?				413			
Yes	90.2% (46)	85.3% (197)	33.6% (44)	287	18.19 (6.75-49.03)***	0.63 (0.23-1.70)	11.46 (6.75-19.15)***
No	9.8% (5)	14.7% (34)	66.4% (87)	126	Reference	Ref.	Ref.
Would you search on the internet for information about the MPV?				393			
Yes, probably or certainly	76.6% (36)	74.2% (164)	52.0% (65)	265	3.02 (1.41-6.47)**	0.88 (0.42-1.84)	2.66 (1.67-4.22)***
No, probably or certainly not	23.4% (11)	25.8% (57)	48.0% (60)	128	Ref.	Ref.	Ref.
Would you visit the following website for information about the MPV?							
National institute for Public Health and the Environment (RIVM)				265			
Yes	83.3% (30)	74.4% (122)	58.5% (38)	190	3.55 (1.30-9.71)*	0.58 (0.23-1.49)	2.06 (1.13-3.78)*
No	16.7% (6)	25.6% (42)	41.5% (27)	75	Ref.	Ref.	Ref.
Dutch Christian Patient Association (NPV)				265			
Yes	30.6% (11)	45.1% (74)	44.6% (29)	114	0.55 (0.23-1.29)	1.87 (0.86-4.05)	1.02 (0.57-1.82)
No	69.4% (25)	54.9% (90)	55.4% (36)	151	Ref.	Ref.	Ref.
Vaccine critical website (Dutch Association for Critical Vaccination and/or Vaccine Free Foundation)				265			
Yes	11.1% (4)	25.6% (42)	78.5% (51)	97	0.03 (0.01-0.11)***	2.75 (0.92-8.25)	0.10 (0.05-0.19)***
No	88.89 (32)	74.4% (122)	21.5% (14)	168	Ref.	Ref.	Ref.

Table 2. Univariate multinomial logistic regression models: association of intention to accept maternal pertussis vaccination with needs from the orientation stage among orthodox Protestant women (N=414) (continued)

	Intention to accept maternal pertussis vaccination (MPV) [a]				MLR Acceptors vs. refusers COR (95%CI)	MLR Undecided women vs. acceptors COR (95%CI)	MLR Undecided women vs. refusers COR (95%CI)
	Acceptors, % (n)	**Undecided women**, % (n)	**Refusers**, % (n)	n			
Would you like to hear or read information about MPV from the following health visions?							
Homeopathy				414			
Yes	2.0% (1)	15.2% (35)	38.6% (51)	87	0.03 (0.00-0.24)**	8.93 (1.19-66.76)*	0.28 (0.17-0.47)***
No	98.0% (50)	84.8% (196)	61.4% (81)	327	Ref.	Ref.	Ref.
Natural medicine				414			
Yes	3.9% (2)	15.6% (36)	45.5% (60)	98	0.05 (0.01-0.21)***	4.52 (1.05-19.44)*	0.22 (0.14-0.36)***
No	96.1% (49)	84.4% (195)	54.5% (72)	316	Ref.	Ref.	Ref.
Would you like to hear or read experiences of other women about their decision to accept or refuse MPV?				412			
Yes	41.2% (21)	69.6% (160)	38.9% (51)	232	1.10 (0.57-2.12)	3.27 (1.75-6.10)***	3.59 (2.29-5.62)***
No	58.8% (30)	30.4% (70)	61.1% (80)	180	Ref.	Ref.	Ref.
Conversation Needs							
How would you discuss this vaccination with your husband/partner?				336			
We probably will discuss this vaccination using the collected information	70.5% (31)	90.2% (165)	56.0% (61)	257	1.88 (0.89-3.97)	3.84 (1.71-8.64)**	7.21 (3.90-13.36)***
We probably will not discuss this vaccination, or not extensively	29.5% (13)	9.8% (18)	44.0% (48)	79	Ref.	Ref.	Ref.

Table 2. Univariate multinomial logistic regression models: association of intention to accept maternal pertussis vaccination with needs from the orientation stage among orthodox Protestant women (N=414) (continued)

	Intention to accept maternal pertussis vaccination (MPV) [a]				MLR **Acceptors vs. refusers** COR (95%CI)	MLR **Undecided women vs. acceptors** COR (95%CI)	MLR **Undecided women vs. refusers** COR (95%CI)
	Acceptors, % (n)	**Undecided women**, % (n)	**Refusers**, % (n)	n			
Would you have a conversation with other people about the MPV?				414			
Yes	78.4% (40)	90.5% (209)	82.6% (109)	358	0.77 (0.34-1.72)	2.61 (1.18-5.81)*	2.01 (1.07-3.76)*
No	21.6% (11)	9.5% (22)	17.4% (23)	56	Ref.	Ref.	Ref.
Would you like to join a group meeting about the MPV?				386			
Yes, probably or certainly	31.3% (15)	42.7% (91)	16.0% (20)	126	2.39 (1.10-5.18)*	1.64 (0.84-3.20)	3.92 (2.26-6.79)***
No, probably or certainly not	68.8% (33)	57.3% (122)	84.0% (105)	260	Ref.	Ref.	Ref.
Needs from health care professional (HCP)							
Would you like an explanation about the pros and cons of the MPV from your midwife?				407			
Yes, probably or certainly	92.0% (46)	92.6% (212)	52.3% (67)	325	10.47 (3.56-30.80)***	1.08 (0.35-3.37)	11.35 (6.21-20.76)***
No, probably or certainly not	8.0% (4)	7.4% (17)	47.7% (61)	82	Ref.	Ref.	Ref.
Would you like an explanation about the pros and cons of the MPV from the child health clinic physician?				401			
Yes, probably or certainly	86.0% (43)	73.5% (164)	35.9% (46)	253	10.95 (4.56-26.31)***	0.45 (0.19-1.06)	4.96 (3.10-7.91)***
No, probably or certainly not	14.0% (7)	26.5% (59)	64.1% (82)	148	Ref.	Ref.	Ref.

Table 2. Univariate multinomial logistic regression models: association of intention to accept maternal pertussis vaccination with needs from the orientation stage among orthodox Protestant women (N=414) (continued)

	Intention to accept maternal pertussis vaccination (MPV) [a]				MLR **Acceptors vs. refusers** COR (95%CI)	MLR **Undecided women vs. acceptors** COR (95%CI)	MLR **Undecided women vs. refusers** COR (95%CI)
	Acceptors, % (n)	**Undecided women**, % (n)	**Refusers**, % (n)	n			
Would you like a personal advice from your midwife?				397			
Yes, probably or certainly	84.3% (43)	78.0% (174)	35.0% (43)	260	10.00 (4.31-23.18)***	0.66 (0.29-1.50)	6.61 (4.06-10.76)***
No, probably or certainly not	15.7% (8)	22.0% (49)	65.0% (80)	137	Ref.	Ref.	Ref.
Would you like a personal advice from the child health clinic physician?				393			
Yes, probably or certainly	76.0% (38)	52.8% (114)	18.9% (24)	176	13.59 (6.19-29.84)***	0.35 (0.18-0.71)**	4.80 (2.86-8.06)***
No, probably or certainly not	24.0% (12)	47.2% (102)	81.1% (103)	217	Ref.	Ref.	Ref.

Abbreviations: MLR=multinomial logistic regression model; COR= crude odds ratio; CI= confidence interval [a] n=414

* p<.05, ** p<.01, *** p<.001

Using factor analysis, three main domains in the deliberation stage were identified based on 11 valuebased statements: 'Trust in the vaccine and vaccine-providing authorities', 'Individual deliberate decision-making' and 'Contemplating religious arguments' (Supplementary material; Table S2 and S3).

Box 1 shows an overview of the deliberation domains and the comprising value-based statements.

Box 1. Deliberation domains and their 11 value-based statements

Trust in vaccine and vaccine-providing authorities
- I am confident that the person who provides the MPV, carefully weighed the pros and cons for me
- I often consider information provided by the government not to be one-sided and not too focused on accepting vaccination
- I do not want to consider other possibilities than vaccination to protect my baby against pertussis
- I consider this vaccination as a justified mean which I may use in gratitude

Individual deliberate decision-making
- I want to know what the pros and cons of the MPV are before I make a decision
- I want to organize my thoughts on the pros and cons of the MPV before I make a decision
- As a Christian, I am personally responsible to make a decision about the MPV
- I try to imagine the consequences if I chose for accepting or refusing MPV

Contemplating religious arguments
- I prayerfully present my decision to God and seek for answers in the Bible
- My decision has to be compatible with my faith in God
- I want to be able to justify my decision to God

The sociodemographic variables that were statistically significantly associated with the intention to vaccinate in the univariate analysis, and therefore included as potentially confounding factor in the multivariate multinomial logistic regression model, were: church denomination, living in an orthodox Protestant municipality, having children, childhood vaccination status of the participant, and personal experience with pertussis (participant had pertussis herself and/or had had close contact with pertussis) (Supplementary material; Table S4). An association between MPV intention and vaccination status of child(ren) could not be determined due to highly skewed distribution over the categories. Yet, it is interesting to note that the MPV intention among acceptors and refusers was in line with their decision to accept or refuse childhood vaccinations for their child(ren) (Supplementary material; Table S4). Concerning personal experience with pertussis, participants who knew a close contact with pertussis were significantly more often refuser than acceptor or undecided about accepting MPV. Women who had pertussis themselves were more often refuser than undecided about accepting MPV.

Probably these findings mainly reflect the objections to vaccination in their social circles (Supplementary material; Table S4).

Results of the univariate multinomial logistic regression analyses showed that all deliberation domains were significantly associated with intention (Supplementary material; Table S5). The multivariable analysis found that acceptors scored significantly higher on the deliberation domain Trust in the vaccine and vaccine-providing authorities, compared to undecided women and refusers (Table 3). Additionally, undecided women scored significantly higher on this trust-related deliberation domain than refusers. On the deliberation domain Individual deliberate decision-making, undecided women showed a significantly higher score than refusers. On this deliberation domain no differences were found among acceptors and refusers, and acceptors and undecided women. In the univariate analysis, refusers scored significantly higher on Contemplating religious arguments than undecided woman and acceptors, and undecided women scored higher on this deliberation domain than acceptors. In the multivariable analysis, no significant differences on Contemplating religious arguments were found among acceptors, undecided women, and refusers, indicating that the need to contemplate religious values was equal among acceptors, undecided women, and refusers.

Table 3. Multivariate multinomial logistic regression analysis: intention to accept MPV and deliberation domains among orthodox Protestant women (N=305) [1]

	Acceptors vs. refusers AOR (95%CI)	Undecided women vs. acceptors AOR (95%CI)	Undecided women vs. refusers AOR (95%CI)
Deliberation domains			
Trust in the vaccine and vaccine-providing authorities [a, #]	37.53 (16.24-86.72)***	0.16 (0.09-0.32)***	6.16 (3.68-10.31)***
Individual deliberate decision-making [b, #]	2.26 (0.997-5.13)	1.35 (0.71-2.55)	3.05 (1.76-5.28)***
Contemplating religious arguments [c, #]	0.79 (0.38-1.63)	0.83 (0.47-1.45)	0.66 (0.41-1.06)

Reported values are controlled for church denomination, living in an orthodox Protestant municipality, having children, participant's childhood vaccination status, participant had pertussis herself, and participant knew close contact with pertussis.

Abbreviations: AOR= Adjusted odds ratio; CI=confidence interval

[1] Missing cases were deleted listwise. [a] n=374, [b] n= 411, [c] n=446. [#] = One-unit increase *** p<.001

Discussion

In this section, we reflect on the study findings following the MPV decision-making framework and discuss implications for intervention development.

Measuring women's intention to accept MPV showed that more than half of the participants (56%) was undecided whether they would accept or refuse the MPV if their HCP would offer this vaccination during pregnancy. Assuming that not all undecided women will accept the vaccination if being offered, supplemented by the 12% of the women that indicated they would certainly accept the MPV, it is expected that the MPV coverage among orthodox Protestant women is substantially less than the MPV coverage of 70% in the general population of Dutch women.[11]

Among women with children, 52% (130/248) was undecided about accepting MPV, among women without children this was 61% (101/166). However, among the subgroups of MPV acceptors (12%) and refusers (32%), we found that their MPV intention complied with their earlier decision to accept or refuse childhood vaccinations for their children. Although this may be a pronounced result, not many studies have determined this association. Yet, in line with our finding, Lefebvre et al. (2019) found in a large sample of French women, that intention to accept MPV was negatively associated with ever refusing a vaccine in the past.[31]

In the orientation stage, acceptors and undecided women showed higher general information needs and needs concerning HCPs, compared to refusers. This finding is supported by previous MPV studies.[32, 33] Strikingly, despite the fact that refusers were certain that they would not accept the MPV, 52% of this subgroup would search the internet for information. However, this does not entail that acceptors, undecided women, and refusers want to search for the same information. Meppelink et al. (2019) showed that the participants in their online health information study perceived belief-confirming vaccination messages -e.g. information that confirms one's existing ideas or beliefs about vaccination- as more credible, useful, and convincing than belief-inconsistent vaccination messages.[34] This is consistent with the finding in our study that refusers showed more interest in the information provided by vaccine-critical websites (79%) and/or alternative health sources (i.e. homeopathy and natural medicine (39% and 46%)) than acceptors and undecided women. The latter was explained in our previously conducted qualitative study. Women clarified that they wanted to use vaccine-critical information and alternative health sources to answer their questions which would not be answered in pro-vaccination information provided by the government.[23] The desire of orthodox Protestants to receive both religious and (non-governmental) health information about vaccination and vaccine

decision-making has also been noted in relation childhood vaccinations and COVID-19 vaccination.[35-37]

Orthodox protestant women in this study showed a high need to talk with other people in their social network about the vaccination. This need was highest among undecided women (91%), followed by refusers (83%). The result that women attribute an important role to family and friends as information source or as sounding board in their decision-making process has also been found in other studies.[18, 23, 38-40] However, to our knowledge, this is the first study showing that women who are undecided about their decision have a higher need to talk to others in their social network as part of their vaccine decision-making process, then acceptors and refusers.

Three deliberation domains in the deliberation stage could be identified from the value-based statements using factor analysis. The deliberation domain Trust in the vaccine and vaccine-providing authorities was found to be the strongest predictor of intention, with acceptors showing the highest trust and refusers the lowest trust. This result reflects findings from earlier studies, showing that vaccine acceptance is strongly associated with trust and/or confidence in vaccine providers, vaccine policymakers, and/or the government.[14, 41-44] Additionally, comparable to our result, a recent study showed that conservative Protestants (evangelical Protestants) in the United States - who believe that the Bible is the literal word of God - have a lower confidence in the COVID-19 vaccination, and a lower vaccine uptake.[45]

Undecided women scored higher on Individual deliberate decision-making than refusers, yet, no difference was found between refusers and acceptors. In contrast with our findings, other studies showed that refusers experienced a higher need to deliberate over pros and cons and the consequences of vaccinations, compared to acceptors who often consider vaccinations as self-evident.[19, 46-48] Taking into account that MPV refusers in this study are more often a member of a conservative church denomination, they may consider refusing vaccinations -instead of accepting- as self-evident, influenced by the social norm and tradition in their community.[22, 25]

The timing of this study can be considered both as a strength and a limitation. Since data collection was conducted prior to the introduction of the MPV in the Dutch immunisation programme, we were able to determine women's intention, needs, and values in the decisions-making process before their decision-making was affected by the national immunisation campaign and standardised procedures and interventions. On the other hand, intention, needs, and values may change when a pregnant woman is actually being offered the vaccination. The results of this study on intention to

accept MPV and the expected decision-making process do not provide data on the decision-making process and actual vaccine acceptance at the time MPV is being offered to the woman during her pregnancy. Another limitation of the study was that no validated scale could be used to assess the value-based deliberation stage as no such scale is available yet.

To select a random sample of participants, we used a wide range of methods to approach women for participation. The characteristics of the study sample were found to be representative for the Dutch orthodox Protestant women of fertile age regarding; church denomination membership, living in an orthodox Protestant municipality or not, and childhood vaccination status compared to the national mean. [20-22] Nonetheless, women with a low education level are underrepresented in this study, a common phenomenon in vaccine-related voluntary sample studies.[12, 19, 49-51] Despite our observation that no association was found between intention and education level, this underrepresentation makes the results less generalizable for lower educated orthodox Protestant women. A previous study on vaccine acceptance among Dutch orthodox Protestants indicated that higher education is associated with higher vaccine acceptance.[22] It is therefore possible that the percentage of MPV refusers among women in the Dutch orthodox Protestant community is higher than found in this study.

Conclusion

Investigating the MPV decision-making process among a religious vaccine-hesitant subgroup shows that the majority of the women has high information needs and wants to conversate with HCPs, friends, and family about the vaccination. Acceptors and undecided women have the highest information needs and needs concerning the HCP, undecided women showed the highest conversation needs, and refusers showed the highest need to visit vaccine-critical websites and receive information from alternative health sources. Concerning the deliberation domains in the deliberation stage, acceptors score highest on Trust in the vaccine and vaccine-providing authorities and undecided women show a higher score on Individual deliberate decision-making than refusers. In the multivariable logistic regression analysis, no differences among acceptors, undecided women, and refusers were found on Contemplating religious arguments, indicating orthodox Protestant women find this domain equally important.

Recommendations

We advise HCPs to verify among all orthodox Protestant pregnant women their decision-making needs, considering we found information needs among all subgroups: acceptors, undecided women, and refusers. The use of open, non-

judgemental conversation techniques by HCPs can assist women who struggle in their decision-making process. For example, by addressing a woman's concerns and exchanging options and ideas how she can search for information or talk about the vaccination with their husband, friends, and family. Additionally, HCPs can help women clarify values that are important to them, which may help the women to guide themselves in reaching a final deliberate decision to accept or refuse MPV. Additionally, insights in the decision-making process of a vaccine-hesitant subgroup can be of great importance in general nationwide maternal vaccination campaigns. Conducting similar studies among other vaccine-hesitant subgroups may result in more tailored information and consultation, and may contribute to the overall optimisation of vaccine health care.

Declarations

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

We wish to thank all people who assisted in the recruitment of study participants.

Funding

This research study was supported by the research fund of the Dutch National Institute for Public Health and the Environment (RIVM), the Netherlands, for local Public Health Services. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Data availability

Data will be made available on request.

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Supplementary materials

- File S1. Partially included in this thesis. Available online at https://view.officeapps.live.com/op/view.aspx?src=https%3A%2F%2Fars.els-cdn.com%2Fcontent%2Fimage%2F1-s2.0-S0264410X22009240-mmc1.xlsx&wdOrigin=BROWSELINK
- Table S1. Frequency tables information needs, conversation needs and needs from HCP (n=467). Table is presented below.
- Table S2. Summary of factor analysis results for the value-based statements in the deliberation stage (n=348). Not included in this thesis.
- Table S3. Frequency tables value deliberation statements (n=348). Not included in this thesis.
- Table S4. Univariate multinomial logistic regression models with intention to accept maternal pertussis vaccination and sociodemographic variables (n=414). Table is presented below.
- Table S5. Univariate multinomial logistic regression models with intention to accept maternal pertussis vaccination and deliberation domains. Table is presented below.
- File S2. Appendix 1. Questionnaire Decision-making on maternal pertussis vaccination (PDF). Not included in this. Available online at https://ars.els-cdn.com/content/image/1-s2.0-S0264410X22009240-mmc2.pdf
- File S3. Appendix 2. Questionnaire in Dutch “Besluitvorming over vaccinaties tijdens en rondom de zwangerschap”. Not included in this. Available online at https://ars.els-cdn.com/content/image/1-s2.0-S0264410X22009240-mmc3.pdf
- File S4. Appendix 3. Data analysis factor analysis and deliberation domain calculation. Not included in this. Available online at https://ars.els-cdn.com/content/image/1-s2.0-S0264410X22009240-mmc4.pdf

File S1.1. Table S1. Frequency tables information needs, conversation needs and needs from HCP (n=467)

	N	%
Information needs		
Would you like to receive information about the MPV during pregnancy?	**466**	
Yes	340	73.0%
Which information about pertussis would you like to receive?	**341**	
Chance of getting pertussis	270	79.2%
Symptoms of pertussis (e.g. coughing, shortness of breath)	172	50.4%
Danger of pertussis (e.g. chance of hospitalization or death)	274	80.4%
Possible ways to prevent pertussis	240	70.4%
How much breastfeeding protects against pertussis	190	55.7%
How much healthy nutrition protects against pertussis	145	42.5%
Which information about MPV would you like to receive?	**341**	
How well the vaccination protects against pertussis	250	73.3%
How the vaccinations works in the body of the pregnant woman and the unborn baby	272	79.8%
What follow-up vaccinations the baby needs when he/she is born	188	55.1%
What side effects a pregnant women can get from the vaccination?	273	80.1%
What negative consequences the vaccination can have for the baby	313	91.8%
What negative long-term consequences the vaccination can have	270	79.2%
What substances the vaccination contains	170	49.9%
What the costs of the vaccination are for the pregnant women herself	110	32.3%
In what form would you like to receive the MPV information?	**341**	
Folder / Brochure	267	78.3%
One or multiple website(s)	162	47.5%
Digital decision-making aid (website which helps you to make a decision)	80	23.5%
Campaign provided by the government	13	3.8%
Movie	69	20.2%
App	16	4.7%
Do you search The Internet for information about this vaccination?	**439**	
Yes, certainly	125	28.6%
Yes, probably	172	39.4%
No, probably not	106	24.3%
No, certainly not	34	7.8%
What website(s) about this vaccination would you visit? Website of...	297	
National association of midwives	130	43.8%
National Institute for Public Health and the Environment (RIVM)	215	72.4%
Dutch Christian patient organization (NPV)	130	43.8%

File S1.1. Table S1. Frequency tables information needs, conversation needs and needs from HCP (n=467) (continued)

	N	%
Vaccine critical website (Dutch Association for Critical Vaccination and/or Vaccine Free Foundation)	105	35.4%
Organisation with an orthodox Protestant / Christian background	82	27.6%
Newspaper or magazine	18	6.1%
Regional public health service (GGD) or child health clinic	162	54.5%
Forum, blog, Twitter or Facebook (social media)	28	9.4%
From what health viewpoint(s) would you like to hear or read more information about the MPV?	**467**	
Homeopathy	96	20.6%
Natural medicine	110	23.6%
Anthroposophy	23	4.9%
None of the above	308	66.0%
Would you like to hear or read experiences of other women about their decision to accept or refuse MPV vaccination?	**465**	
Yes	265	57.0%
From which women would you like to hear or read these experiences?	267	
Women with a similar religious background	179	67.0%
Women with a similar way of thinking about health	169	63.3%
Women in my immediate surroundings	131	49.1%
Conversation needs		
How would you discuss the whooping cough vaccination with your husband (or partner)?	**378**	
We probably will not talk about this vaccination together. We have already made our decision on whether or not to vaccinate	50	13.2%
We will not talk about this vaccination in detail. My husband often leaves decisions about vaccinations up to me	32	8.5%
I will tell him what I know about the vaccination and then we will make our decision together whether or not to vaccinate	138	36.5%
We look together for information pro and against vaccination and we then make a decision together about whether or not to vaccinate	158	41.8%
With which people would you discuss the vaccination?	**467**	
I do not want to discuss the vaccination with others	61	13.1%
Female friends	303	64.9%
(male) friends	84	18.0%
(other) pregnant women	203	43.5%
Sisters	215	46.0%
Parents	215	46.0%
Other family members	79	16.9%
Colleagues	78	16.7%
Acquaintances from church	99	21.2%

File S1.1. Table S1. Frequency tables information needs, conversation needs and needs from HCP (n=467) (continued)

	N	%
Imagine, you are pregnant and in your neighbourhood there is a group meeting about het MPV. The group meeting provides information about the MPV, it is possible to ask questions and you can talk with other women about the MPV.		
Would you join such a group meeting?	**430**	
Yes, certainly	31	7.2%
Yes, probably	113	26.3%
No, probably not	180	41.9%
No, certainly not	106	24.7%
Which party do you prefer for the organisation of the group meeting?	**144**	
Midwife	45	31.3%
Dutch Christian patient organization (NPV)	31	21.5%
other orthodox Protestant / Christian organisation	26	18.1%
Regional public health service (GGD) or Child Health Clinic	17	11.8%
National Institute for Public Health and the Environment (RIVM)	13	9.0%
Dutch Association for Critical Vaccination (NVKP)	8	5.6%
Other	4	2.8%
Needs from health care provider		
In the course of 2019 all pregnant women are being offered a MPV. The vaccination will be provided during pregnancy by a physician of the child health clinic. Would you like to receive…		
an explanation from your midwife about the pros and cons of the vaccination?	**460**	
Yes, certainly	274	59.6%
Yes, probably	102	22.2%
No, probably not	46	10.0%
No, certainly not	38	8.3%
an explanation from the physician of the child health clinic about the pros and cons of the vaccination?	**452**	
Yes, certainly	193	42.7%
Yes, probably	104	23.0%
No, probably not	87	19.2%
No, certainly not	68	15.0%
personal advice from your midwife?	**477**	
Yes, certainly	178	39.8%
Yes, probably	121	27.1%
No, probably not	83	18.6%
No, certainly not	65	14.5%

File S1.1. Table S1. Frequency tables information needs, conversation needs and needs from HCP (n=467) (continued)

	N	%
personal advice from the physician of the child health clinic	**411**	
Yes, certainly	107	24.3%
Yes, probably	100	22.7%
No, probably not	138	31.3%
No, certainly not	96	21.8%

File S1.2. Table S4. Univariate multinomial logistic regression models with intention to accept maternal pertussis vaccination and sociodemographic variables (n=414)

	Intention to accept maternal pertussis vaccination (MPV) [a]				**MLR Acceptors vs. refusers** COR (95%CI)	**MLR Undecided women vs. acceptors** COR (95%CI)	**MLR Undecided women vs. refusers** COR (95%CI)
	Acceptors, % (n)	**Undecided women**, % (n)	**Refusers**, % (n)	n			
Age, in years				**414**			
18-22	15.7% (8)	26.0 % (60)				1.88 (0.68-5.16)	1.50 (0.77-2.92)
23-28	39.2% (20)	30.3% (70)	25.8% (34)	124	1.59 (0.64-3.95)	0.88 (0.37-2.05)	1.39 (0.74-2.63)
29-34	25.5% (13)	26.4% (61)	33.3% (44)	118	0.80 (0.31-2.07)	1.17 (0.47-2.93)	0.94 (0.50-1.75)
35-40	19.6% (10)	17.3% (40)	20.5% (27)	77	Reference	Ref.	Ref.
Education				**414**			
Low education level [x]	3.9% (2)	3.9% (9)	7.6% (10)	21	0.40 (0.08-1.97)	0.99 (0.20-4.88)	0.40 (0.15-1.04)
Intermediate education level [+]	49.0% (25)	48.9% (113)	56.1% (74)	212	0.68 (0.35-1.32)	1.00 (0.54-1.85)	0.67 (0.43-1.05)
High education level [#]	47.1% (24)	47.2% (109)	36.4% (48)	181	Ref.	Ref.	Ref.
Church denomination				**414**			
Protestants with orthodox Prot. affinity [d]	31.4% (16)	18.6% (43)	13.6% (18)	77	40.00 (4.93-324.34)**	0.16 (0.02-1.29)	6.32 (2.89-13.85)***
Low level of conservatism [c]	33.3% (17)	19.9% (46)	8.3% (11)	74	69.55 (8.33-580.43)***	0.16 (0.02-1.29)	11.07 (4.67-26.23)***
Moderate level of conservatism [b]	33.3% (17)	54.1% (125)	43.9% (58)	200	13.19 (1.69-102.87)*	0.43 (0.05-3.46)	5.71 (3.01-10.81)***
High level of conservatism [a]	2.0% (1)	7.4% (17)	34.1% (45)	63	Ref.	Ref.	Ref.
Living in an orthodox Protestant municipality				**402**			
No, living in a municipality with <5% votes for SGP	40.0% (20)	26.7% (60)	22.8% (29)	109	2.25 (1.12-4.54)*	0.55 (0.29-1.03)	1.23 (0.74-2.04)
Yes, living in a municipality with ≥5% votes for SGP	60.0% (30)	73.3% (165)	77.2% (98)	293	Ref.	Ref.	Ref.

File S1.2. Table S4. Univariate multinomial logistic regression models with intention to accept maternal pertussis vaccination and sociodemographic variables (n=414) (continued)

	Intention to accept maternal pertussis vaccination (MPV) [a]				MLR **Acceptors vs. refusers** COR (95%CI)	MLR **Undecided women vs. acceptors** COR (95%CI)	MLR **Undecided women vs. refusers** COR (95%CI)
	Acceptors, % (n)	**Undecided women**, % (n)	**Refusers**, % (n)	n			
Relationship status				**414**			
No partner/husband	13.7% (7)	19.9% (46)	12.9% (17)	70	1.08 (0.42-2.77)	1.56 (0.66-3.70)	1.68 (0.92-3.07)
Partner/husband	86.3 (44)	80.1% (185)	87.1% (115)	344	Ref.	Ref.	Ref.
Having children				**414**			
No	45.1% (23)	43.7% (101)	31.8% (42)	166	1.76 (0.91-3.41)	0.95 (0.51-1.74)	1.67 (1.06-2.61)*
Yes	54.9% (28)	56.3% (130)	68.2% (90)	248	Ref.	Ref.	Ref.
Number of children				**248**			
1	35.7% (10)	23.8% (31)	23.3% (21)	62	3.65 (0.88-15.09)	0.39 (0.10-1.57)	1.42 (0.64-3.14)
2	32.1% (9)	35.4% (46)	27.8% (25)	80	2.76 (0.66-11.47)	0.64 (0.16-2.58)	1.76 (0.83-3.74)
3	21.4% (6)	22.3% (29)	23.3% (21)	56	2.19 (0.49-9.89)	0.60 (0.14-2.68)	1.32 (0.59-2.95)
4 or more	10.7% (3)	18.5% (24)	25.6% (23)	50	Ref.	Ref.	Ref.
Pregnancy status				**391**			
Not pregnant	70.2% (33)	79.0% (173)	76.0% (95)	301	0.74 (0.35-1.57)	1.60 (0.79-3.23)	1.19 (0.70-2.01)
Pregnant	29.8% (14)	21.0% (46)	24.0% (30)	90	Ref.	Ref.	Ref.
Childhood vaccination status of the participant				**410**			
Not vaccinated	9.8% (5)	28.6% (65)	59.8% (79)	149	0.07 (0.03-0.18)***	3.68 (1.39-9.73)**	0.25 (0.16-0.40)***
Partially vaccinated	9.8% (5)	7.5% (17)	6.8% (9)	31	0.60 (0.18-1.93)	0.96 (0.34-2.76)	0.57 (0.24-1.38)
Completely vaccinated	80.4% (41)	63.9% (145)	33.3% (44)	230	Ref.	Ref.	Ref.

File S1.2. Table S4. Univariate multinomial logistic regression models with intention to accept maternal pertussis vaccination and sociodemographic variables (n=414) (continued)

	Intention to accept maternal pertussis vaccination (MPV) [a]				MLR **Acceptors vs. refusers** COR (95%CI)	MLR **Undecided women vs. acceptors** COR (95%CI)	MLR **Undecided women vs. refusers** COR (95%CI)
	Acceptors, % (n)	**Undecided women**, % (n)	**Refusers**, % (n)	n			
Childhood vaccination status of partner				**322**			
Not vaccinated	7.1% (3)	33.9% (57)	45.5% (51)	111	0.08 (0.02-0.27)***	6.66 (1.96-22.67)**	0.51 (0.30-0.85)*
Partially vaccinated	11.9% (5)	8.3% (14)	15.2% (17)	36	0.38 (0.13-1.14)	0.98 (0.33-2.93)	0.37 (0.17-0.83)*
Completely vaccinated	81.0% (34)	57.7% (97)	39.3% (44)	175	Ref.	Ref.	Ref.
Vaccination status of child(ren)				**246**	*Due to highly skewed distribution over the categories, no univariate multinomial logistic regression model could be calculated*		
Not vaccinated	0% (0)	13.2% (17)	68.5% (61)	78			
Partially vaccinated	0% (0)	16.3% (21)	23.6% (21)	42			
Completely vaccinated	100% (28)	70.5% (91)	7.9% (7)	126			
Vaccination intention for future child(ren)				**132**	*Due to highly skewed distribution over the categories, no univariate multinomial logistic regression model could be calculated*		
Intended to accept no childhood vaccination	0% (0)	13.0% (10)	90.9% (30)	40			
Intended to accept some childhood vaccinations	13.6% (3)	40.3% (31)	3.0% (1)	35			
Intended to accept all childhood vaccination	86.4% (19)	46.8% (36)	6.1% (2)	57			

File S1.2. Table S4. Univariate multinomial logistic regression models with intention to accept maternal pertussis vaccination and sociodemographic variables (n=414) (continued)

	Intention to accept maternal pertussis vaccination (MPV) [a]				MLR **Acceptors vs. refusers** COR (95%CI)	MLR **Undecided women vs. acceptors** COR (95%CI)	MLR **Undecided women vs. refusers** COR (95%CI)
	Acceptors, % (n)	**Undecided women**, % (n)	**Refusers**, % (n)	n			
Personal experiences with pertussis: Participant had pertussis herself				**414**			
No	86.3% (44)	85.3% (197)	72.7% (96)	337	2.36 (0.97-5.71)	0.92 (0.38-2.22)	2.18 (1.28-3.69)**
Yes	13.7% (7)	14.7% (34)	27.3% (36)	77	Ref.	Ref.	Ref.
Personal experiences with pertussis: Child(ren) had pertussis				**414**	*Due to highly skewed distribution over the categories, no univariate multinomial logistic regression model could be calculated*		
No	100% (51)	95.7% (221)	82.6% (109)	381			
Yes	0% (0)	4.3% (10)	17.4% (23)	33			
Personal experiences with pertussis: Participant knew close contact with pertussis				**414**			
No	80.4% (41)	66.7% (154)	49.2% (65)	260	4.23 (1.96-9.14)***	0.49 (0.23-1.03)	2.06 (1.33-3.19)**
Yes	19.6% (10)	33.3% (77)	50.8% (67)	154	Ref.	Ref.	Ref.

Abbreviations: COR= crude odds ratio; CI= confidence interval; MPV= maternal pertussis vaccination; SGP = Staatkundig Gereformeerde Partij (political party)

[a] n=414

[x] No, primary or prevocational education

[+] Secondary or secondary vocational education [#] Higher professional education or university

[a] Reformed Congregations in the Netherlands (GGiN), Old Reformed Congregations (OGG)

[b] Reformed Congregations (GG) or Restored Reformed Church (HHK)

[c] Christian Reformed Churches (CGK) or Reformed Bond (within Protestant Church in the Netherlands) * p<.05, ** p<.01, *** p<.001

File S1.3. Table S5. Univariate multinomial logistic regression models with intention to accept maternal pertussis vaccination and deliberation domains

Deliberation domains	n	Acceptors vs. refusers AOR (95%CI)	Undecided women vs. acceptors AOR (95%CI)	Undecided women vs. refusers AOR (95%CI)
Trust in the vaccine and vaccine-providing authorities [#]	340	37.53 (16.24-86.72)***	0.16 (0.09-0.32)***	6.16 (3.68-10.31)***
Individual deliberate decision-making [#]	391	2.26 (0.997-5.13)	1.35 (0.71-2.55)	3.05 (1.76-5.28)***
Contemplating religious arguments [#]	397	0.79 (0.38-1.63)	0.83 (0.47-1.45)	0.66 (0.41-1.06)

Abbreviations: AOR = adjusted odds ratio; CI=confidence interval

[#] = One-unit increase *** p<.001

Chapter 7

General discussion

The overall aim of this thesis was to gain insight into vaccine decision-making processes of orthodox Protestants and to obtain more in-depth understanding of factors related to vaccination acceptance of adolescent and adult vaccinations in this group.

After a general introduction in **Chapter 1**, **Chapter 2** describes an ecological database-study on HPV-vaccination aimed at determining under-vaccinated subgroups. Besides girls living in municipalities with high voting proportions for conservative Protestant political parties, other under-vaccinated subgroups found in this study were: girls of foreign ethnicity, girls living in areas with lower socioeconomic status, and girls living in municipalities with high voting proportions for populist political parties with liberal-conservative views.

In **Chapter 3**, a case-control study on measles susceptibility among unvaccinated orthodox Protestants, we found that adolescents and young adults who -during a measles epidemic in childhood- did not reside in orthodox Protestant strongholds, did not attend an orthodox Protestant primary school, had no older siblings and belonged to a moderately conservative church were more at risk of contracting measles at older age, with an increased risk of complications.

In **Chapter 4**, a mixed-methods study among unvaccinated orthodox Protestant women showed that most participants had personal experience with rubella, few participants considered themselves susceptible to rubella, and more than half of the women were undecided whether to accept rubella susceptibility screening or rubella vaccination if needed.

A qualitative study on maternal pertussis vaccination decision-making, described in **Chapter 5**, identified that the decision-making process of orthodox Protestant women includes different stages and needs for decision-making. We developed a theoretical framework on the vaccine decision-making process based on the perspective of orthodox Protestant women. Following the vaccination offer, the orientation stage reflects women's information and conversation needs. The deliberation stage includes women's contemplation and their weighing of pros and cons based on values they consider important regarding vaccination.

In **Chapter 6**, we quantified the vaccine decision-making framework and found that orthodox Protestant women generally expect to have high information needs, conversation needs, and needs concerning the health care provider (HCP) in their vaccine decision-making process. Concerning these needs in the orientation stage, both similarities and differences were found among acceptors, undecided women, and

refusers. Additionally, three deliberation domains were identified in the deliberation stage: *trust in the vaccine and vaccine-providing authorities*, *individual deliberate decision-making*, and *contemplating religious arguments*. Acceptors scored highest on the deliberation domain *trust in the vaccine and vaccine-providing authorities*. Undecided women showed a higher score on *individual deliberate decision-making* than refusers. No difference was found among women concerning *contemplating religious arguments*.

In this final chapter, **Chapter 7**, I first discuss our findings on vaccine decision-making from the perspective of the individual in a broader context, based on our vaccine decision-making framework and needs for decision-making. Next, I discuss informed and deliberate decision-making by the individual versus the public health goal of increasing vaccination coverage. Subsequently, I discuss methodological considerations on the studies in this thesis. Finally, I outline the implications and recommendations for public health practice, vaccine policy-makers and future research.

Vaccine decision-making from the individual's perspective

Our decision-making framework is unique in that it is designed from the perspective of the person who has to make the vaccination decision (Figure 1). Our framework extends from the moment the woman is offered the vaccination till the moment she has decided to either accept or refuse the vaccination. The vaccination offer is followed by an orientation and deliberation stage. In the orientation stage, women indicated that they would like to receive and search for information to learn more about the vaccination and the disease it prevents, and to gain a better understanding about the decision they would have to make (Chapter 5). Additionally, women wanted to conversate with others -including their husband, friends, family and their HCP- to assemble opinions, information, and experiences about the vaccination issue. In the deliberation stage, women desired a moment to contemplate the pros and cons of a decision based on values they consider important. Although the framework commences with an orientation stage followed by a deliberation stage, these stages do not necessarily have to follow in a consecutive order and may coexist simultaneously. In comparison, McNeil et al. (2019) visualise coexisting stages -sources of influence and deliberate processes- in their vaccine decision-making model as a cogwheel in which parents' perceived advantages and disadvantages of childhood vaccinations, motivation, experiences, and value-based and practical reasons 'why to vaccinate' and 'why not to vaccinate' interact.[1] Therefore, I too presume that many orthodox Protestant women meander between the orientation and deliberation stage before they reach a final decision. In summary, our framework

visualises a personally-driven decision-making process, in which individuals indicate how they reach a well-considered decision to accept or refuse vaccination.

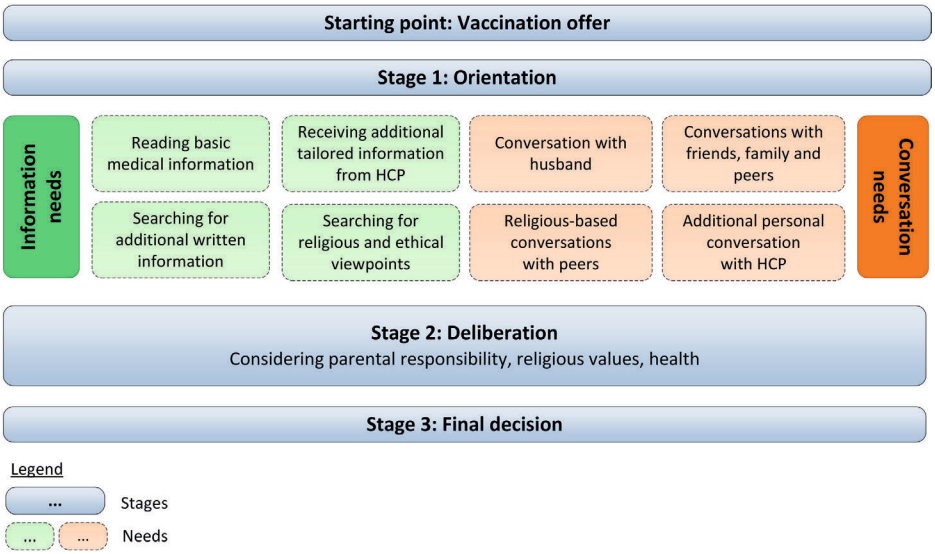

Figure 1. Framework of decision-making process on maternal pertussis vaccination among orthodox Protestant women

The findings of the study described in Chapter 5 show that most orthodox Protestant women aim to make an informed and deliberate vaccination decision. Previously published literature contains several studies on informed decision-making and on deliberate decision-making. Some researchers consider a decision to be informed when the decision-maker has sufficient, accurate, evidence-based knowledge on the offered vaccination and the infectious disease it prevents.[2-4] Other researchers describe informed decision-making as the feeling of the decision-maker of being sufficiently informed on the options, risks and benefits of the vaccination to be able to make a decision.[5-8] The few studies that have been published on deliberate decision-making agree that this concept involves conscious consideration of pros and cons of accepting and refusing vaccination.[1, 9, 10] Furthermore, informed and deliberate decision-making are often described as being interrelated, as information and knowledge influence deliberation and vice versa.[1, 2, 4] Taken from the individual's perspective, only decision-makers themselves can determine whether they have enough information and have deliberated sufficiently to make a decision regarding vaccination. In this general discussion, I refer to the individual decision-making process of orthodox Protestant women as an informed and deliberate decision-making process, as I consider this term most accurately describes the full scope of the process.

For HCPs, the vaccine decision-making framework provides a glimpse on how orthodox Protestant women want to reach a vaccination decision. Additionally, the framework contains concrete leads on how HCPs can support these women in their vaccine decision-making process: by providing medical information, by offering tailored information and by offering a personal conversation to discuss the vaccination issue. In comparison, shared decision-making (SDM) is an approach described from the perspective of HCPs that aims to better support patients in making the best decision between different treatment options.[11] The decision support stages in the SDM model – providing information, supporting deliberation and stimulating patients to make a preference-based decision – align well with the information and conversation needs and the different stages in our vaccine decision-making framework.[11, 12] Therefore, I believe that combining elements of the SDM method and the vaccine decision-making framework can improve HCP's support in vaccine decision-making. However, it is important to mention that a SDM process assumes two or more decision options. In vaccine decision-making there are two decision options: to vaccinate or not to vaccinate, and based on the loyalty to their professional mandate to prevent illness and protect public health, HCPs probably consider refusing vaccination inferior to accepting vaccination.[12] Nevertheless, the HCP's skills from the SDM approach, such as active listening, discussing risks and benefits, letting patients explain what is most important to them in their decision, and following the patient's stages of decision-making, can be beneficial in supporting individuals to make an informed and deliberate vaccination decision.

Vaccination offer as starting point of decision-making

Vaccination offers for vaccinations in de National Immunisation Programme are usually personal invitations by mail from the National Institute for Public Health. However, as pregnancy status is not registered nationally, pregnant women are informed on the maternal pertussis vaccination offer by their midwife. Therefore, as described by our orthodox Protestant participants, the vaccine decision-making process concerning this vaccination starts at the midwife's office.

All orthodox Protestant women, including those who pointed out that they would probably refuse the vaccination based on religious grounds, wanted to be explicitly informed about the vaccination option (Chapter 5). HCPs may -unintentionally or intentionally- withhold a vaccination offer. Some women indicated that if they did not receive the vaccination offer, they would not be able to make their own decision. In general, orthodox Protestants highly value autonomy in vaccination decision-making, as they feel they have to justify their decision before God.[10, 13, 14] To ensure decision-making autonomy, it is important that everyone who is eligible for

the vaccination, receives an explicit vaccination offer so they can initiate their own individual vaccine decision-making process.[15]

Importance of information in vaccine decision-making

In the Netherlands, information on vaccinations is provided to those who are eligible to receive a vaccination from the National Immunisation Programme. This information is generated by the government and national public health institute, and disseminated through online and offline channels. Additional verbal information is also often provided by HCPs. Orthodox Protestant women indicated they considered both written and verbal information important in their vaccine decision-making process (Chapters 4, 5 and 6).

In our mixed-methods study on rubella screening and rubella vaccination (Chapter 4), we found that many unvaccinated women never received information about rubella, rubella screening or rubella vaccination from their midwife or another HCP. For practical reasons, rubella screening is offered during pregnancy by antenatal care providers to unvaccinated women only. Interviews with orthodox Protestant participants revealed that in the absence of information, women tend to rely on knowledge about rubella from personal experience. Moreover, this personal experience strongly influences their intention to accept rubella screening or vaccination. For example, some women considered rubella protection unnecessary because they presumed they had had rubella as a child, and because of the absence of recent rubella outbreaks. The review of Karafillakis et al. (2017) showed that vaccination concerns are strongly influenced by perceptions of low likelihood of contracting vaccine-preventable diseases, their perceived low severity, and overall lack of information.[16] Based on the high information need, and the desire of orthodox Protestant women to make an individual vaccination decision, I propose that all unvaccinated women of childbearing age should receive information on rubella, rubella vaccination, and potential susceptibility to enable them to make an informed decision on rubella screening and catch-up vaccination.

As described in Chapter 5, most women expected the information from a HCP to be focused primarily on the benefits of vaccination and to be insufficient to answer all of their questions, resulting in the need to search for additional information themselves. Additional self-search for information to answer personal questions regarding vaccination is a commonly found need in the vaccine decision-making process.[17-19] The Internet has gained great popularity among vaccine information seekers, including orthodox Protestants (Chapter 6), who aim to find balanced information tailored to their situation. Several studies show that many individuals consider both information based on empirical evidence and anecdotal information applicable

and informative to their situation.[4, 18] Focus groups among parents indicated that parents were seeking information about the positive and negative experiences they might have in the event of choosing to, or choosing not to, vaccinate their child, rather than understanding or comparing complicated numerical information on risks and benefits.[20] The content of anti-vaccination messages is often based on personal experiences, anecdotes and storytelling.[21] These vaccine-critical anecdotal messages receive significant public attention on The Internet and social media platforms.[22] Nonetheless, by understanding the popularity of these narrative messages and using these storytelling strategies on epidemiological and science-based information, HCPs and vaccine-policy makers can tailor their information to better connect to individuals' information needs.[23]

Many orthodox Protestant participants believed that the government's information on maternal pertussis vaccination would mainly cover the advantages of vaccination (Chapter 5), a belief that was also found among non-orthodox Protestant parents concerning childhood vaccinations.[18] Some parents think governments or HCPs withhold information on the negative effects of vaccination to prevent them from refusing vaccination.[18, 24] In their search for information from different sources, individuals can easily end up with non-scientifically proven vaccine-critical information.[25, 26] In response to minimize vaccine hesitancy and refusal, many HCPs and policy-makers feel the need to combat vaccine critical 'misinformation' by removing this information from The Internet.[27] It is important to acknowledge that removing misinformation does not solve the decision-maker's need to search for information from different sources. Therefore, I argue that individuals' need for information should be better addressed by tailoring information to the concerns of specific target groups. For orthodox Protestants, for example, a vaccination information brochure about childhood vaccinations was developed that discusses vaccination from both medical and religious perspective.[28] In 2013, the brochure was widely distributed among orthodox Protestants during the measles epidemic. Interviews revealed that years later orthodox Protestant women were still familiar with this brochure (Chapter 5). The brochure was revised during the COVID-19 pandemic to include COVID-19 vaccination, vaccine development, and HPV-vaccination.[14] In the United States, project COVIDLATINO was launched to well-inform ethnic minorities during the pandemic. The project provided digitally culturally tailored, evidence-based, critical and timely COVID-19 information in short animations in several languages.[29] These promising examples of tailored information may address the information needs of many individuals, preventing them from reading and believing misinformation.

Besides a perceived lack of information, individuals may also have limited access to information. Our study on HPV-vaccination uptake indicated lower vaccination

uptakes among individuals of foreign ethnicity and individuals living in areas with a lower socioeconomic status, where generally more low literacy individuals reside (Chapter 2). Reasons why individuals in these subgroups may have a lower vaccination uptake is that they do not (fully) understand the vaccination offer or the provided vaccination information.[30, 31] Several studies showed that individuals with a lower socioeconomic status and/or a foreign ethnicity are more often unaware of a recommended vaccination.[32-34] In the Netherlands, information about childhood and adolescent vaccination and maternal pertussis vaccination is provided in several languages, yet, this information is not adapted to people with lower literacy levels.[35] In 2022, the Dutch government intends to develop and provide tailored information -in terms of form and content- to people with a low socioeconomic status, with a migration background or a specific religious background.[36] These interventions aim to increase the vaccination coverage among these subgroups and increase health benefits. Moreover, they will increase the opportunity for these individuals to make an informed vaccination decision.

Importance of conversation in vaccine decision-making

In addition to information needs, we found that orthodox Protestant women feel the need to conversate with their husband, friends, family, and peers in order to make a well-considered decision (Chapter 5 and 6). As also found in other studies, individuals decide which people in their social network they want to consult to talk about vaccination.[37-42] They use these conversations as a source of information and to broaden their perspective regarding the vaccination. Research showed that using friends and family as a source of information is associated with having vaccination concerns.[43, 44] These studies do not clarify whether conversating with friends or family members causes vaccination concerns, or whether individuals conversate with friends and family because they have pre-existing vaccination concerns. Regardless, the need for conversation in the vaccine decision-making process shows that these needs should not be ignored. Therefore, I believe that HCPs should encourage individuals who feel the need to do so to talk about their vaccination decision with trusted friends and family members, as this may clarify their personal vaccination perspective.

Both our studies and other studies have found that individuals value conversations with HCPs in their vaccine decision-making process.[18, 45-47] In line with our findings among orthodox Protestant women (Chapter 5 and 6), many individuals who have to make a vaccination decision prefer a direct conversation and may be disappointed if HCPs do not have sufficient time to further discuss the topic after a vaccination offer.[18, 48] The review of Ames et al. (2017) indicates that parents expect longer-then-usual appointments; clear answers to their questions; information tailored

to their needs; and open discussions in which HCPs were helpful, caring, sensitive and receptive to their concerns.[18] Therefore, it is important that HCPs have sufficient time and knowledge to meet these conversation needs.

An open, non-judgmental approach of HCPs in vaccination conversations was found to be important by orthodox Protestant women (Chapter 5), but also among non-orthodox Protestant parents.[18, 49] Additionally, several studies indicate that both parents and HCPs found it important that the HCP's opinion on vaccination should not influence a parent's decision (Chapter 5).[18, 50, 51] Nevertheless, a systematic review showed that HCPs who are not vaccinated themselves were less motivated to advice patients to receive a vaccination.[52] A Belgian study on maternal pertussis vaccination found that for some women the main reason for not being vaccinated was that vaccination was discouraged by their HCP.[53] These studies indicate that HCPs -unintentionally or intentionally- can influence an individual's vaccination decision. The desire among orthodox Protestant women to be able to make an individual vaccination decision implies they prefer a participatory communication approach, in which the HCP initiates a dialogue about the vaccination and in which the vaccination is presented as optional, rather than a presumptive communication approach, in which the HCP starts the dialogue by stating that the vaccination will be provided at the end of the consultation and does not initiate a vaccination conversation.[54]

Hitherto, the relationship between the -participatory or presumptive- approach of HCPs and vaccine decision-making is unclear. As the use of presumptive communication in vaccination consultations results in higher vaccination uptakes than the participatory approach, some researchers consider the presumptive approach a more promising intervention strategy in vaccination care than the participatory approach.[55-58] Since most individuals are expected to be vaccine accepting, HCPs are recommended to initiate the vaccination conversation with the presumptive approach, and if the individual has questions or concerns about vaccination, the HCP can change to a more nuanced communication technique, still promoting vaccine acceptance.[59]. However, none of the studies on using the presumptive approach in vaccination care measured decision contentment or influence of this approach on the vaccine decision-making process. Williamson et al. (2018) raises an ethical concern, that presumptive communication is used to 'nudge' individuals towards accepting vaccination without their knowledge, even though they have a choice to refuse vaccination.[60] Taken into account that orthodox Protestant women (Chapter 5) disliked any form of nudging by their HCP, the presumptive approach can also have a counterproductive effect and undermine trust between the individual and the HCP. In my opinion, based on these thesis findings, it is essential to critically examine the effect of the participatory and presumptive approaches on informed and deliberate

individual decision-making from the perspective of the individual, before conclusions can be drawn about the effect of either approach.

Deliberation in vaccine decision-making

In chapter 5, we found that a time out for deliberation on the vaccination issue is an important component of the vaccine decision-making process for orthodox Protestant women. This deliberation stage can be described as a cognitive process of weighing pros and cons based on values women consider important in relation to the vaccination decision. Current literature contains only minimal emphasis on deliberation in vaccine decision-making by individuals. Studies describing deliberation in vaccine decision-making provide a narrow explanation of this process and refer to deliberation as the process of weighing pros and cons [1, 2, 4, 61] or considering consequences of vaccinating and non-vaccinating [2]. McNeil et al. (2019), moreover, define values that can be important to the individual, e.g. responsibility, social altruism, safety and trust, as components in the deliberative process in vaccine decision-making.[1]

Chapter 6 provides more insight into the deliberation stage by identifying the deliberation domains orthodox Protestant women consider important in deliberation. In the study's questionnaire women were asked to respond to statements given in the interviews and online focus groups in the qualitative study (Chapter 5), which resulted in three deliberation domains: *trust in the vaccine and vaccineproviding authorities*, *individual deliberate decision-making*, and *contemplating religious arguments* (Chapter 6). Elements of these deliberation domains were also found in the vaccine decision-making process of other subgroups and populations. As found in our study, trust in the safety and efficacy of vaccines, trust in those who administer vaccines or give advice on vaccination, and trust in the wider health care system is largely recognised as an important factor in the vaccine decision-making process.[62-65] The deliberation domain *individual deliberate decision-making* refers to the need and perceived responsibility to personally weigh pros and cons, and to imagining the consequences of the decision to either accept or refuse vaccination. As also found in other studies describing this form of deliberation, this domains mainly refers to the process of deliberation, rather than the content of the pros and cons, e.g. to prevent infection or concerns about side effects.[1, 2, 4, 61] The deliberation domain *Consideration of religious arguments* in vaccine decision-making seems natural for individuals for whom religious or philosophical beliefs are an important part of their daily lives. However, the role of religious or philosophical considerations in vaccine decision-making is addressed in only a few studies.[66-68] Overall, I suggest that a greater focus in future research on the role of religious, philosophical and other personal values in deliberation processes can provide starting points for supporting individuals who experience difficulties in their vaccine decision-making process.

In this thesis, we found that personal values affect a vaccination decision (Chapter 5 and 6). As many individuals find it difficult to develop an informed and deliberate vaccination decision, in which they take their personal values in account, values clarification methods could be helpful. Values clarification methods aim to help individuals clarify and communicate personal values while guiding them through the decision-making process.[69] Several studies suggest that values clarification methods can reduce decisional conflict in vaccine decision-making, as individuals were more confident about their vaccination decision [70], made a decision more in accordance with their values, and were more certain about their decision [7, 71]. Given the desire for value deliberation among orthodox Protestant women in the decision-making process, vaccine-hesitant individuals in this subgroup may benefit from a values clarification method. However, for this method to be beneficial, it is important that the full broad spectrum of values, including religious or philosophical values, are accounted for. Cataldi et al. (2019) attempted to include a wide range of values, including religious values, in their Parental Vaccine Values scale to determine parents' values in vaccine decision-making.[72] A combination of this Parental Vaccine Values scale and existing values clarification methods may be helpful and could be part of the development of a vaccination deliberation support aid.

Individual informed and deliberate decision-making versus public health aims to increase vaccination acceptance

Personal autonomy and freedom of choice in individual decision-making are highly valued in Western societies.[73] Yet, individual decisions cannot be seen outside of the context of society, as choices are determined and influenced by this society and have an impact on society.[74] Autonomy in vaccine decision-making and the freedom to make an informed, considered decision are not isolated issues, as vaccine refusal creates tension between individual choices and public health.[60] When insufficient individuals choose to accept a vaccination, the vaccination coverage may not reach the necessary herd immunity levels to prevent disease outbreaks. As a result, the need of individuals to reach their own informed and deliberate decision can conflict with vaccine policies aimed at high vaccination acceptance to sustain herd immunity.[75]

In formulating a vaccination policy, a government or public health authority must first determine which goal is being pursued. Subsequently, it must be assessed which intervention will be most effective to achieve the intended goal. In many cases, this goal will be a high vaccination coverage, as this reduces the risk of infectious disease outbreaks and, thus, benefits public health. However, to aim for a high vaccination coverage does not necessarily eliminate the goal of providing the opportunity for individual decision-making.

When implementing vaccine-promoting interventions, it is important for governments and policy-makers to determine the impact of these interventions on individual decision-making. The principle of least restrictive alternative (PLRA) states that if two interventions can both efficaciously and effectively address a public health or health policy issue, the intervention least restrictive of personal liberties ought to be preferred.[76] Based on this principle, compulsory vaccination was found to be most restricting on individual's liberty and autonomy, followed by disincentives (penalties), incentives and nudging. Vaccination policies based on persuasion, for example providing information emphasizing the benefits of vaccination, were found to be least restricting.[76] However, it is important to consider that vaccine-hesitant individuals may already perceive information and communication messages as methods that pressure them to accept vaccination.[18] Interventions such as compulsory vaccination, disincentives, incentives, nudging and persuasion may increase vaccination acceptance [77], however, they may also negatively impact individual autonomy and freedom. Bardosh et al. (2022) showed that interventions intended as incentives or nudges to accept COVID-19 vaccination were viewed as freedom-restricting by substantial proportions of the population, resulting in counterproductive and damaging effects to public health and vaccine confidence.[78] This emphasizes the need for governments and vaccine-policy makers to carefully consider vaccine promoting interventions, as a countereffect may result in a trust gap between individuals and authorities or HCPs.[79]

Individuals and subgroups with higher distrust in governments and scientific or public health institutions show more reluctance to vaccine promotion interventions.[63, 80, 81] These under-vaccinated subgroups with lower levels of trust in governments and health systems include subgroups with populist or conservative right-winged ideology, and religious and ethnic minorities.[63, 82-86] Although lower vaccine uptakes have been established among these groups, little is known about their needs for vaccine decision-making. Therefore, I believe it is important to gain understanding on the vaccine decision-making process among these vaccine hesitant groups and to investigate how and by whom they want to be supported in their vaccination decision, and whether they are amenable to this support. Subsequently, this knowledge can be used to tailor vaccination information and decision-making support to reduce countereffects of vaccine promoting interventions including vaccine resistance among these groups.

Methodological reflections

A main strength of this thesis is the combination of both qualitative and quantitative studies, enabling us to explore the underlying concepts of and argumentation in

vaccine decision-making and acceptance, and to measure how these concepts relate to each other in the decision-making process.

The orthodox Protestant community is a known hard-to-reach subgroup. However, by using knowledge from previous studies among the orthodox Protestant community, we experienced no difficulty to recruit sufficient participants for our studies. As a result, all studies involved a sufficient number of respondents to reach data saturation (Chapter 4 and 5) and large enough sample sizes (Chapter 3, 4 and 6).

In the qualitative maternal pertussis vaccination study (Chapter 5), we were able to develop a vaccine decision-making framework based on the findings derived from our multi-method approach of data collection and data analysis. The interviews were used to explore the individual decision-making process; the interview results, literature search, and research group meetings were used to construct a concept framework; and subsequently, the online focus groups were used to gain deeper insight into the stages and corresponding decision-making needs in the framework.

The asynchronous focus groups took place on a password protected forum over a five-day period of time. The forum had the advantage of anonymity among the participants, and participants had sufficient time to consider our questions and their responses to the researchers and other participants. They also had more time to influence each other's thinking patterns through their shared comments. As this is a natural and unintentional process, we were not able to determine what the effect of this influence might have been on the study results. What may have influenced the results was that, due to the asynchronous setting of the focus group, women could determine how much time they wanted to spend of the forum. Women with more available time and women who were more involved in the study or the subject were more active in the forum, therefore, it is probable we gained more insight into the vaccine decision-making process from these women than from women with less active participation.

The studies on maternal pertussis vaccination (Chapter 5 and 6) were conducted prior to the implementation of the maternal pertussis vaccination in the national immunisation programme. During the interviews most women were unaware of the option of pertussis vaccination during pregnancy and were somewhat overwhelmed by the information on this topic. Compared to the interview participants, online focus group participants had more time to carefully think about their prospected decision-making process if they were offered a maternal pertussis vaccination in the future compared, which contributed to the reliability and completeness of the findings. On the one hand, questioning decision-making on a hypothetical situation

allowed women to be more honest and open about their decision-making without feeling additional social desirability effects. On the other hand, due to the timing of these studies, women had to hypothesize how they would think and behave in an unfamiliar future situation, which some women found challenging. Nevertheless, it does reflect the actual situation when an individual receives a vaccination offer; the starting point of the decision-making process. Therefore, our research provides important knowledge to understanding the process of decision-making. However, it also emphasizes the importance to conduct research among individuals at the time they are in the respective situation and actually going through the decision-making process.

In the studies among orthodox Protestant women, we had a response bias concerning education level. Due to the lack of sufficient participants with lower levels of education, the decision-making process of these individuals may not be adequately reflected in the findings of Chapter 4, 5 and 6. Additionally, although we intentionally focused these studies on women, as they are considered the primary main decision-maker regarding maternal pertussis vaccination, the results do not reflect the decision-making needs of men.

Except for the database-study (Chapter 2), we conducted our studies in a subgroup of orthodox Protestants, which is small yet significant for safeguarding herd-immunity against infectious disease outbreaks in the Netherlands. The specific characteristics of orthodox Protestants and their religious-based lifestyle make it difficult to extrapolate the data to other groups or populations. Nonetheless, when comparing our findings with other vaccine decision-making studies among vaccine-hesitant populations, many similarities are found. This indicates that our results may be more generalizable than previously thought. However, this can only be concluded if our vaccine decision-making framework is examined and compared in other subgroups. Preferably, therefore, a follow-up study will examine whether orthodox Protestant women completed the decision-making process as they had previously intended, and whether they had the same or different needs as anticipated in advance. These findings can then be used to improve the framework, if necessary.

Implications for practice, policy and future research

Even though the Dutch orthodox Protestants community is a small under-vaccinated subgroup, knowledge gained in this thesis about this subgroup on informed and deliberate decision-making can be used to improve vaccine decision-making support. The findings of this thesis lead to recommendations for public health practice, policy and future research. These recommendations apply to the group studied, on the one

hand, and to other under-vaccinated subgroups and vaccine-hesitant individuals, on the other.

Recommendations for public health practice and policy

For the Dutch orthodox Protestants the following is recommended based on studies and considerations in the general discussion in this thesis:

- The government and national public health authority must facilitate an explicit vaccination offer and additional information on the vaccination and the disease it prevents to each individual who is eligible for the vaccination. This provides individuals with the opportunity to decide for themselves whether or not to accept the vaccination. If the vaccination offer is related to the individual's health status, such as pregnancy, which is unknown to the government or national public health authority, the offer should be made by the relevant HCPs, such as midwife or general practitioner. The vaccination offer and additional information should be given in plain language. Furthermore, the offer should be objective and non-judgemental.
- The government and national public health authority should offer catch-up vaccination to unvaccinated individuals who have not been infected with measles or rubella in the past. This recommendation is particularly applicable to orthodox Protestants but can also apply to individuals from other under-vaccinated groups. Due to unfamiliarity with persistent susceptibility, unvaccinated individuals may not be aware they are still susceptible and therefore at risk for these diseases and their complications. Unvaccinated adolescents and adults should be made aware of these risks by HCPs with knowledge and experience on this subject, followed by an offer to screen for susceptibility and, if necessary, a measles-mumps-rubella (MMR)-vaccination offer. From a medical and practical point of view it is possible to offer MMR-vaccination without susceptibility screening, however, unvaccinated individuals may be less inclined to accept an 'unnecessary' vaccination.
- There are several occasions in which information, screening, catch-up vaccination and, if desired by the decision-maker, decision-making support can be offered by HCPs to unvaccinated individuals so the individual can make a personal vaccination decision:
    - Midwives and gynaecologists should discuss MMR-vaccination status and potential rubella susceptibility with all women during pregnancy and offer screening to unvaccinated women. As MMR-vaccination cannot be administered during pregnancy, women susceptible to rubella should be reminded about the vaccination offer after pregnancy by this HCP.

    - Travel physicians can discuss MMR-vaccination status and risk for measles and rubella infection during travel abroad and at home with men and women attending a travel-related health consultation.
    - Less common, but nonetheless optional, is a vaccination offer to parents who decide to have their child vaccinated and indicate that they have not been vaccinated themselves. When the physician who facilitates vaccinations for the child is not able to administer vaccinations for adults, they can refer the parent to the family physician or regional public health institute.
    - The Dutch government intends to reorganize vaccination care in the Netherlands, and to entrust the administration of vaccinations in the hands of one health care party.[36, 87] HCPs who are less familiar with measles and rubella susceptibility can refer unvaccinated individuals to this organisation for information, screening, catch-up vaccinations and decision-making support in the future.
- The above mentioned recommendations focus on the time period when no outbreak is occurring. As orthodox Protestants indicated they would be more inclined to decide on vaccination during an emerging outbreak (Chapter 4), governments and public health institution should prepare information and vaccination campaigns in anticipation of an upcoming measles or rubella outbreak. Tailored vaccination information materials should be developed focused on informing potentially susceptible unvaccinated individuals. Additionally, instructions should be prepared to inform relevant HCPs on how and when to offer catch-up MMR-vaccination and decision-making support.
- HCPs involved in vaccination care and working in the Bible belt area should gain knowledge of our vaccine decision-making framework to better understand orthodox Protestants' vaccine decision-making process and to help them identify their needs for decision-making. The following tools can be added to the framework to better support informed and deliberate decision-making:
    - HCP's skills included in the shared decision-making approach, such as active listening, discussing risks and benefits and letting patients explain what is most important to them, should be applied in vaccination consultations, if desired by the decision-maker.
    - Values clarification methods can be used if individuals are unable to balance their pros and cons or clarity which values matter most to them in the vaccination decision.
    - HCPs who are responsible for administering vaccinations must provide individuals sufficient time for their decision-making process, as for some deciding about vaccination is a thorough and extensive process in which they do not want to be rushed.

- To ensure that HCPs can support individuals in informed and deliberate decision-making, governments and policy-makers must provide relevant HCPs with the necessary resources, including sufficient time, education opportunity, facilities and finances.

Based on the knowledge gained in this thesis on the orthodox Protestants and its usefulness for improving practice and policy regarding vaccine decision making and acceptance in this under-vaccinated group, it is recommended that governments, and national and regional health care institutes gain insight into the underlying causes of vaccine hesitancy in under-vaccinated subgroups and their vaccine decision-making process. This knowledge should be used to tailor vaccination information and decision-making support to these groups and vaccine-hesitant individuals.

Recommendations for future research

In this thesis, we determined and visualised the vaccine decision-making process of orthodox Protestant women in a framework. This framework can be used to gain insights into the vaccine decision-making process and needs of other vaccine-hesitant individuals and under-vaccinated subgroups as well. Therefore, the following is recommended:

- Explorative research should be conducted to determine whether our vaccine decision-making framework is applicable to other vaccine-hesitant individuals and under-vaccinated subgroups, including the subgroups found in Chapter 2: individuals with foreign ethnicity, lower socioeconomic status (lower education and/or lower literacy levels), and populist or conservative right-winged political ideology. This research should also focus on individuals who favour alternative medical philosophies as they are known to highly value informed and deliberate decision-making.[66, 88, 89] These studies should explore the information and conversation needs in vaccine decision-making among these groups and individuals, as this knowledge can be used to tailor vaccine decision-making support.
- The cognitive process of deliberation needs further investigation, including how weighing pros and cons and values are integral to the deliberation stage. Research should reveal whether and how values clarification methods can support individual vaccine decision-making. These studies should include consideration of religious and philosophical values, as these values can strongly influence the vaccine decision-making process of individuals with religious and philosophical beliefs.
- Given that shared decision-making is considered an effective approach to support decision-making, and this approach shares similarities with our vaccine decision-

making framework, future research should explore whether combining elements of the SDM method and the vaccine decision-making framework can improve HCP's support in vaccine decision-making, followed by an investigation on the impact of the new HCP's support on informed and deliberate decision-making among vaccine-hesitant individuals.

- In preparation for an upcoming vaccine preventable disease outbreak where a new vaccine or an existing vaccination will be offered to a new target population, it is useful to examine perceived needs of individuals with respect to vaccine decision-making in the hypothetical situation of a vaccination offer. Studies should be performed to confirm these results in the situation of an actual offer.

Final conclusion

The discussion of this thesis focusses on the vaccine decision-making process of orthodox Protestant women from an individual's perspective. In a framework, we visualise the decision-making process starting with a vaccination offer, followed by an orientation and deliberation stage. Women aim to make an informed and deliberate decision by addressing their needs for information and conversation and by deliberation of pros and cons based on values they consider important in their decision to either accept or refuse vaccination. To improve vaccine decision-making support, vaccination offers and vaccination information should not primarily focus on promoting vaccination but must be aligned with informed and deliberate decision-making and individual's needs for decision-making. As informed and deliberate decision-making may also be important among other vaccine-hesitant individuals and other under-vaccinated subgroups, this should be further investigated.

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Chapter 8

Appendices

Summary
Samenvatting
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Summary

The orthodox Protestant community in the Netherlands is traditionally known as an under-vaccinated subgroup and thus at risk of infectious disease outbreaks. Although a fair amount is known about the vaccination coverage among the orthodox Protestant community, little is known about their vaccine decision-making process. Therefore, this thesis aims to gain insight into vaccination decision-making process of orthodox Protestants from the individual's perspective and to obtain more in-depth understanding of factors related to vaccination acceptance concerning adolescent and adult vaccinations in this group.

Chapter 2 outlines the orthodox Protestant community in perspective to other under-vaccinated groups. Using an ecological database study among girls who were invited for HPV-vaccination, we found that it is not only girls who live in municipalities with high voting proportions for conservative Protestant political parties, generally known as orthodox Protestant strongholds, that have a lower HPV-vaccination uptake. Other under-vaccinated subgroups are: girls of foreign ethnicity, girls living in areas with lower socioeconomic status, and girls living in municipalities with high voting proportions for populist political parties with liberal-conservative views.

Acquiring measles at a later age poses an increased risk of complications. In a case-control study (**Chapter 3**) we identified the characteristics of unvaccinated orthodox Protestant adolescents and young adults who escaped infection during the measles epidemic of 1999/2000 and got infected with measles during the epidemic of 2013/2014. We found that adolescents and adults who -during a measles epidemic in childhood- did not reside in orthodox Protestant strongholds, did not attend an orthodox Protestant primary school, had no older siblings and belonged to a moderately conservative church were more at risk of contracting measles at older age, with an increased risk of complications.

Rubella infection during early pregnancy can cause severe complications in the unborn child. Therefore, unvaccinated women of childbearing age are advised rubella susceptibility screening and, if they are still susceptible, rubella vaccination. A mixed-methods study combining an online survey and semi-structured interviews among unvaccinated orthodox Protestant women (**Chapter 4**) indicated that only few women were offered rubella screening during pregnancy, and most participants did not consider themselves susceptible to rubella, although no laboratory screening had been conducted. In addition, more than half of the women were undecided whether to accept rubella susceptibility screening or rubella vaccination if needed.

The studies in **Chapters 5** and **6** provide insight into the maternal pertussis vaccination decision-making process of orthodox Protestant women. In a qualitative study, we identified that this vaccine decision-making process includes different stages and needs for decision-making (**Chapter 5**). After the vaccination offer, women want to orientate on the vaccination. This orientation stage comprises women's needs to receive information and to converse with others about the vaccination. The next stage, the deliberation stage, includes women's contemplation and their weighing of pros and cons based on values they consider important in the vaccination issue. In **Chapter 6**, a quantitative online survey study, we found that orthodox Protestant women generally have high information needs, conversation needs, and needs concerning health care providers in their vaccine decision-making process. In the deliberation stage, three deliberation domains were identified: *Trust in the vaccine and vaccine-providing authorities*, *Individual deliberate decision-making*, and *Contemplating religious arguments*. Similarities as well as differences were found among acceptors, undecided women, and refusers with regards to information and conversation needs in the orientation stage and deliberation domains in the deliberation stage.

In summary, this thesis identifies subgroups at risk for vaccine preventable diseases at a later age. Moreover, it provides insight into perceived disease susceptibility, intention for vaccination acceptance, needs for decision-making, and an overall understanding of the vaccine decision-making process of orthodox Protestant women and how these women aim to make an informed and deliberate vaccination decision. This knowledge can be used by the Dutch government and national and regional public health institutes to improve vaccination offers, vaccination information and vaccine decision-making support. In addition, it provides direction for future research to gain more understanding about vaccine decision-making from an individual's perspective among other under-vaccinated subgroups.

Samenvatting

De reformatorische gezindte in Nederland staat bekend als een subgroep met een lage vaccinatieacceptatie. Personen die behoren tot de reformatorische gezindte worden ook wel orthodox protestanten genoemd. Ongeveer 60% van de orthodox protestanten is gevaccineerd tegen verschillende kinderziektes conform het Rijksvaccinatieprogramma. Als gevolg van de lage vaccinatiegraad heeft deze groep een verhoogd risico op uitbraken van infectieziekten. Het doel van dit proefschrift is om inzicht te krijgen in het ervaren perspectief van orthodox protestanten op het vaccinatiebesluitvormingsproces. Daarnaast hebben we onderzocht welke factoren van invloed zijn op vaccinatieacceptatie bij vaccinaties voor adolescenten en volwassenen.

De studie in **hoofdstuk 2** toont de acceptatie van de HPV-vaccinatie in de reformatorische gezindte en andere subgroepen met een lage vaccinatiegraad in Nederland. In een ecologische databasestudie onder meisjes die uitgenodigd zijn voor HPV-vaccinatie vonden we dat niet alleen meisjes die in een gemeente wonen waarin meer gestemd wordt op conservatief christelijke politieke partijen een lagere HPV-vaccinatiegraad hebben. Andere subgroepen met een lagere HPV-vaccinatieacceptatie zijn: meisjes van wie één of beide ouders niet geboren zijn in Nederland, meisjes die in een wijk wonen met een lagere sociaaleconomische status en meisjes die in een gemeente wonen waarin meer gestemd wordt op populistische politieke partijen met liberaal-conservatieve opvattingen.

Een persoon die op latere leeftijd besmet wordt met mazelen heeft een verhoogde kans op complicaties. Een case-control onderzoek (**hoofdstuk 3**) beschrijft de kenmerken van ongevaccineerde reformatorische adolescenten en jongvolwassenen die niet op jonge leeftijd besmet zijn met mazelen tijdens de epidemie van 1999/2000, maar mazelen kregen tijdens de epidemie van 2013/2014. Adolescenten en jongvolwassenen die tijdens de mazelenepidemie van 1999/2000 niet in een gemeente met een groot aandeel orthodox protestanten woonden, niet naar een reformatorische basisschool gingen, geen oudere broers of zussen hadden en behoorden tot een gematigd conservatieve reformatorische kerk liepen meer risico om op latere leeftijd mazelen te krijgen. Dit in vergelijking met adolescenten en jongvolwassenen die wel in een gemeente met een groot aandeel orthodox protestanten woonden, wel naar een reformatorische basisschool gingen, oudere broers of zussen hadden en behoorden tot een conservatieve reformatorische kerk in 1999/2000.

Een besmetting met rodehond (rubella) tijdens de vroege zwangerschap kan ernstige complicaties bij het ongeboren kind veroorzaken. Om die reden worden ongevaccineerde vrouwen in de vruchtbare leeftijd aangeraden om zich te laten testen op antistoffen voor rubella. Indien een vrouw geen antistoffen heeft wordt haar geadviseerd zich te laten vaccineren tegen rubella. **Hoofdstuk 4**, een combinatiestudie van online vragenlijsten met interviews onder ongevaccineerde reformatorische vrouwen, laat zien dat weinig vrouwen tijdens de zwangerschap een test op rubella-antistoffen aangeboden kregen. De meeste vrouwen meenden niet vatbaar te zijn voor rubella, hoewel er geen laboratorium screening was uitgevoerd. Meer dan de helft van de vrouwen twijfelde over het accepteren van een rubella-antistoftest of rubellavaccinatie als deze aangeboden zou worden.

De **hoofdstukken 5** en **6** geven inzicht in het besluitvormingsproces van reformatorische vrouwen over de kinkhoestvaccinatie tijdens de zwangerschap. Een kwalitatieve studie laat zien dat dit vaccinatiebesluitvormingsproces uit verschillende stadia bestaat en verschillende besluitvormingsbehoeften omvat (**hoofdstuk 5**). Na het vaccinatieaanbod willen vrouwen zich oriënteren op de vaccinatie. In deze oriëntatiefase hebben vrouwen de behoefte om informatie te ontvangen, informatie te lezen en met anderen over de vaccinatie te praten. In de volgende fase, de overdenkingsfase, willen vrouwen zich op de vaccinatiekeuze beraadslagen en de voor- en nadelen voor zichzelf afwegen op basis van waarden die voor hen belangrijk zijn. In een online vragenlijstonderzoek (**hoofdstuk 6**), vonden we dat reformatorische vrouwen in hun vaccinatiebesluitvormingsproces over het algemeen een grote behoefte hebben aan informatie en gesprekken met bekenden en zorgverleners. In de overdenkingsfase werden drie domeinen geïdentificeerd: *Vertrouwen in de vaccinatie en de vaccinatie-aanbieder, Individuele bewuste besluitvorming* en *Overweging religieuze argumenten*. Er werden zowel overeenkomsten als verschillen gevonden in informatiebehoeften, conversatiebehoeften en overdenkingsdomeinen tussen vrouwen die de kinkhoestvaccinatie zeker wilden accepteren, vrouwen die hier nog over twijfelden en vrouwen die de vaccinatie zeker niet wilden accepteren.

Samengevat identificeert dit proefschrift welke personen een verhoogd risico hebben op een infectieziekte op latere leeftijd en geeft het inzicht over de wijze waarop reformatorische vrouwen geïnformeerde en weloverwogen vaccinatiebesluitvorming hopen te bereiken. Deze kennis kan worden gebruikt door de Nederlandse overheid en landelijke en regionale publieke gezondheidszorgorganisaties in het optimaliseren van het vaccinatieaanbod, de vaccinatie-informatie en de ondersteuning bij vaccinatiebesluitvorming. Daarbij biedt het richting aan toekomstig onderzoek om meer inzicht te krijgen in vaccinatiebesluitvorming vanuit individueel perspectief bij andere subgroepen met een lage vaccinatiegraad.

List of abbreviations

AOR	Adjusted odds ratio
CBS	Statistics Netherlands
CDA	Christian Democratic Appeal
CI	Confidence interval
COR	Crude odds ratio
CU	Christian Union
D66	Democrats 66
DTaP-IPV	Diphtheria-tetanus-pertussis-polio vaccine
FvD	Forum for Democracy
GL	Green Left
HCP	Health care provider
HPV	Human papillomavirus
LVC	Low vaccination coverage
MHS	Municipal Health Services
MLR	Multinomial logistic regression
MPV	Maternal pertussis vaccination
MMR	Measles-mumps-rubella
MPV	Maternal pertussis vaccination
NIP	National Immunisation Programme
OFG	Online focus group
OPD	Orthodox Protestant denomination
OPS	Orthodox Protestant school
OR	Odds ratio
PvdA	Labour Party
PvdD	The Party for the Animals
PVV	Party for Freedom
SCP	The Netherlands Institute for Social Research
SDM	Shared decision-making
SGP	Reformed Political Party
SP	Socialist Party
RPHS	Regional Public Health Service
VPD	Vaccine preventable disease
VVD	People's Party for Freedom and Democracy

Dankwoord

Ik zit in een hobbelige trein in Thailand op weg naar de volgende bestemming. Dit proefschrift is een paar weken geleden goedgekeurd door de manuscriptcommissie. Het ritmische gestommel en de voorbijtrekkende landschappen brengen me terug naar de reis van dit proefschrift en alle mensen die mij geholpen hebben om de eindbestemming te bereiken. Gaandeweg mijn reis door Zuidoost-Azië vult het reisdagboek zich met een dankwoord vol herinneringen aan jullie en hoe belangrijk jullie waren bij het tot stand brengen van dit proefschrift.

Tijdens de proefschriftreis had ik een heel fijn promotieteam dat ik graag als eerste wil bedanken.

Lieve Marlies, wat ben ik blij dat je als promotor mij onder jouw vleugels wilde nemen. Je daagde me uit om de onderzoeken naar een hoger niveau te brengen, met oog voor detail liet je me kritisch nadenken over wat ik nou eigenlijk op papier had gezet en je bracht me in contact met kundige mensen die ons onderzoek konden verrijken. Jouw betrokkenheid, openhartigheid en gedrevenheid heb je ook op mijn proefschriftreis willen loslaten, waar ik heel dankbaar voor ben.

Lieve Rob, jij bent de specialist in het vangen van gedrag en ervaringen in een overzichtelijk model. Dit was heel waardevol in de onderzoeken en bij het beantwoorden van ingewikkelde vragen van reviewers over ons model. Jouw analytische en nuchtere visie maakte complexe ideeën weer concreet. Je zette mijn leerproces centraal en geloofde in mijn eigen kunnen als promovendus. Dank je wel voor dit vertrouwen.

Lieve Jeannine, ik kwam bij jou vol wensen en vragen over het doen van een promotietraject. Dankzij jou is dit ook echt van de grond gekomen via de academische werkplaats AMPHI. Tijdens de proefschriftreis heb je me keer op keer geholpen om mijn gedachtestromen te focussen en om vragen om te zetten in antwoorden. Heel veel dank voor het vertrouwen dat je me hebt gegeven, voor jouw bemoediging op de moeilijke momenten en voor het geduld om mee te denken hoe ik persoonlijke en onderzoeksgerelateerde barrières kon overwinnen.

Lieve Helma, bijna 10 jaar geleden vroeg je mij of ik het misschien leuk vond om samen met jou een onderzoek te doen naar reformatorische jongeren die mazelen hadden gekregen tijdens de epidemie die toen gaande was. Jouw proefschrift en jouw aanstekelijke enthousiasme over de doelgroep legde de basis voor dit proefschrift. Je leerde me dat goed onderzoek doen ook inhoudt dat de resultaten

relevant zijn voor de praktijk. Dank je wel voor het delen van jouw schat aan kennis en de gezellige uitjes naar de studiedagen van het Dutch Bible Belt Network.

Mijn dank gaat uiteraard ook uit naar personen die deel hebben genomen aan de onderzoeken. In het bijzonder de vrouwen die openhartig hun gedachten en ervaringen hebben gedeeld en ons een inkijkje wilden geven in hun wereld.

De proefschriftreis begon bij GGD Gelderland-Zuid. Lieve oud-collega's, we hebben jarenlang fijn samenwerkt in de reizigersadvisering en infectieziektebestrijding. We hebben samen gelachen, gezwoegd en geleerd. Veel dank aan de 'IZB-zusters'; Anke, Ans, Yvonne, Charlotte, Marian, Nico, Marijn, Harmke en Helen, dat jullie mij de ruimte hebben gegeven om naast de diensten ook aan dit onderzoek te kunnen werken. Lieve Karlijn, jij hebt mij enthousiast gemaakt voor de publieke gezondheidszorg. Je bent voor mij een rolmodel hoe je als verpleegkundige vanuit ambitie en motivatie door kan groeien.

Lieve Giovanna, ik heb het je volgens mij best lastig gemaakt met mijn wens om als verpleegkundige en als onderzoeker te willen werken. Dank je wel dit je dit mogelijk hebt gemaakt. In mijn loopbaanzoektocht zag jij misschien wel als eerste dat de combinatie onderzoek en beleid het beste bij mij paste. Dank je wel voor dit inzicht en ik hoop dat ik vanuit mijn huidige functie veel voor jullie kan betekenen.

Lieve Pleun, dank je wel voor de wandelingen en uitjes buiten kantoortijden. Laten we dit vooral blijven voortzetten. En dank voor de attente berichtjes die je precies op de goede momenten weet te sturen.

Ook wil ik GGD'ers uit andere regio's bedanken die geholpen hebben bij het realiseren van dit proefschrift. Toos, dank je wel dat je de meerwaarde zag in dit onderzoek en dat hebt uitgedragen.

Tijdens de proefschriftreis had ik het geluk om de onderzoekscollega's van academische werkplaats AMPHI te ontmoeten en te mogen putten uit hun kennis. Lieve Ellen, Daphne, Daphne, Stijn, Maartje, Loes, Olga, Karlijn en Suzanne dank voor jullie gezelligheid tijdens de bijpraatmomenten en congressen. Lieve Alma, dank je wel voor jouw geduldige uitleg over wat ik nou eigenlijk aan het berekenen was met de logistische regressieanalyse; wat was het nou, controles waren eigenlijk ook cases? Beste Reinier, jij hebt me enorm geholpen bij het ontdekken van associaties in de grote databasestudie. Dank ook aan de studenten die mij geholpen hebben in het onderzoek en uitvoeren van aanvullend literatuuronderzoek. Lieve Dagmar, in

het bijzonder dank aan jou voor onze fijne samenwerking en voor het afnemen van de interviews waarvoor je stad en land moest afreizen.

Lieve Henri en Pieternel, dankzij jullie heb ik de reformatorische doelgroep beter leren kennen. Henri, in 2013 begonnen we zij aan zij aan de mazelentelefoon om patiënten op te sporen, waarbij jij mij bijspijkerde over de levenswijze en gewoonten van de reformatorische gezinnen. Dank je wel dat je bereid was om dit gedurende de hele proefschriftreis te blijven doen. Pieternel, jij in het bijzonder ook veel dank voor het meelezen met de vragenlijsten en de artikelen.

Beste Anke, Rijk, Tessa, Alies, Hester en Susan, dank jullie wel dat ik samen met jullie onderzoek heb mogen doen en voor alles wat ik van jullie geleerd hebt.

In het bijzonder ook dank aan het Dutch Bible Belt Netwerk. Fred van Lieburg en Anneke Pons, jullie hebben Helma en mij altijd met open armen ontvangen op de BBN studiedagen en daarbuiten. Dat we deze bijzondere samenwerking maar door mogen zetten in de toekomst.

Lieve collega's bij GGD GHOR Nederland. Dank jullie wel voor jullie interesse in mijn onderzoek. En dank voor de bemoedigende woorden tijdens de COVID-19 pandemie toen het promotietraject naast onze drukke werkzaamheden me best zwaar viel. Lieve Albertine, jij hebt me warm welkom geheten in een hele bizarre situatie toen COVID-19 Nederland net had bereikt. Je geeft de vereniging een thuisgevoel, dank daarvoor. Lieve Merel, we zijn in najaar 2021 aan elkaar gekoppeld en wat hebben we in deze tijd veel meegemaakt. Dank je wel voor je heerlijke humor die het werk nog leuker maakt. En dank dat je me hebt geholpen om tijd vrij te maken zodat ik in alle hectiek nog een presentatie kon maken of een artikel kon herzien. De volgende keer mag jij een paar maanden op reis. Beste Ton, Martine en Ineke, dank jullie wel voor de ruimte die ik kreeg om mijn onderzoek voort te zetten vanuit GGD GHOR Nederland. Daarnaast ook veel dank dat ik vier maanden vrij kon nemen om op reis te gaan. Ook aan alle andere collega's en andere betrokken op het VIP programma, dank jullie wel voor de fijne samenwerking; op naar de mooiste en beste infectieziektebestrijding in Nederland.

Lieve vrienden en familie, wat ben ik gezegend met zulke lieve, leuke mensen om mij heen. Dank jullie wel voor de interesse in het onderzoek, maar vooral ook voor de ontspanning, gezellige momenten en leuke activiteiten.

Lieve Sjoerd, wat ben ik blij dat we na 35 jaar nog altijd vrienden zijn. Onze plannen toen we kleuters waren om samen een winkel te beginnen is dan misschien niet van

de grond gekomen, maar we zijn evengoed prima terechtgekomen. Op dat we nog maar vaak met Evangeline en Wouter mogen converseren over reizen, werk en het leven onder het genot van een goed glas wijn.

Lieve Pauline, we hebben in ruim 30 jaar vriendschap al veel meegemaakt; leuke, spannende, verdrietige en stoere momenten. Dank je wel dat ik altijd bij je terecht kan.

Lieve muziekvrienden van HKO, The All Weather Band en THUNK!, dank jullie wel voor de gezellige en ontspannen muzikale momenten samen die het leven extra kleur geven. Lieve duikvrienden, de wereld is ook heel mooi onder water. Hopelijk kunnen we daar nog lang samen van genieten.

Lieve Jette en Jeroen, via de muziek hebben we elkaar gevonden, maar zoveel meer samen meegemaakt dan alleen dat. Wat fijn dat jullie weer dichtbij wonen. Op dat er nog maar veel Citroenvlinderkerstdiners mogen volgen.

Lieve Anthonie, Miranda, Rene en Leontine. Jullie hebben ons in Wijchen onthaalt en ons bekend gemaakt met de beste culinaire plekken in Wijchen en omstreken. Speciaal voor jullie heb ik extra voorzichtig gedaan op reis om veilig terug te keren.

Lieve Rodin, Lieke, Yannick en Marloes, dank voor onze vriendschap, jullie interesse in mijn onderzoek en jullie luisterend oor als ik even wilde spuien. Fijn dat we onze passie voor tuinieren kunnen delen en kunnen proosten op deze ecologische hobby. Lieke, opdat onze tenniscarrière maar succesvol mag worden, en mocht dit niet zo uitpakken, dan vinden we vast een nieuwe uitdaging. Lieve Rodin, al bijna 15 jaar zitten we wekelijks naast elkaar. Is het niet in het orkest, dan wel in Aalsburg of Saltshof, dan wel in een lokale horecagelegenheid. Speciaal dank aan jou dat je ook op 8 juni naast me wil staan als paranimf en in de voorbereiding naar deze dag toe. Lieve Julian en Robin, dank jullie wel voor jullie wonderlijke kijk op de wereld.

Lieve Ludo en José, dank jullie wel dat ik onderdeel mag zijn van ‘de Munter-Braem’-familie, en voor jullie betrokkenheid en interesse in mijn onderzoek. Jullie weten dat ik Ilse graag had ontmoet, maar ik ben ook heel dankbaar dat ik José heb leren kennen. Lieve Sophie, Stephanie, Frederick, Bram, Amelie, Gilles, Maxime, Len en Laurie, bedankt voor de weekendjes in Spa, de gezamenlijke uitjes en de etentjes op de Koewacht. Lieve Leonie en Roel, hopelijk volgen er nog vele escaperooms met aansluitende nazit om de overwinning te vieren, of in een heel enkel geval, een troostbiertje te drinken.

Lieve Merthe, dank je wel voor jouw zorgzaamheid, jouw humor en bereidheid om het hele (!) proefschrift mee te lezen op het Engels. Je hebt al vaak aan mijn zijde willen staan bij bijzondere gelegenheden. Dank dat je dat ook deze keer wil doen als mijn paranimf. Bart, Fedde en Thijs, dank voor de gezellige familiemomenten en dat jullie me wegwijs maken in de mannenwereld van bouwen, tractors en dinosaurussen.

Lieve Ada en Bert, lieve pap en mam. Dank jullie wel voor jullie onvoorwaardelijke steun en liefde. Jullie hebben mij de eigenschappen en mogelijkheden meegegeven om dit proefschrift te kunnen schrijven. Het vermogen om door te zetten bij tegenslag, creativiteit en de drijfveer om leuke ideeën tot een mooi einde te brengen. Ada, heel veel dank voor jouw (stille) kracht in het onbaatzuchtig helpen van anderen en het openen van mijn ogen voor andere samenlevingen en culturen. Bert, heel veel dank voor de schilderen van de voorkant voor dit boekje en de afbeeldingen aan de binnenkant.

Lieve, lieve Wouter. Jij was het meest enthousiast toen ik promotieonderzoek wilde gaan doen. Ondanks mijn motivatie en ambitie was de promotieonderzoekreis niet altijd makkelijk. Elke keer als ik wat moedeloos aan de keukentafel zat vol twijfel of ik het allemaal wel ging redden, was jij daar om een dosis positiviteit over me uit te storten en om me ervan te verzekeren dat het allemaal wel goed zou komen. En zie daar, had je toch gelijk. Dankzij jou geniet ik zoveel meer van het leven. Je bent heel belangrijk voor me, ook als ik vele kilometers verderop zit. Ik hoop dat we nog heel veel avonturen samen mogen beleven, boven en onder water. Ik hou duizend van je.

Curriculum Vitae

Anne Mulder werd geboren op 28 maart 1987 te Ede. Na het behalen van haar vwo-diploma aan Het Streek Lyceum te Ede, deed zij een opleiding verpleegkunde aan de Hogeschool van Arnhem en Nijmegen (HAN) te Nijmegen. Vanaf 2010 volgde zij een pre-master en master Klinische gezondheidswetenschappen (masterprogramma Verplegingswetenschap) aan de Universiteit Utrecht. Haar afstudeerthesis deed zij bij de afdeling Plastische Chirurgie van het Radboudumc te Nijmegen, waarna zij haar master in 2013 afrondde.

In de periode 2014-2018 voerde ze het onderzoek 'Wie heeft de (vorige) mazelenepidemie gemist?' uit, vanuit het werkveld infectieziektebestrijding bij GGD Gelderland-Zuid, in samenwerking met academische werkplaats AMPHI, een samenwerkingsverband tussen GGD'en, gemeenten en het Radboudumc.

In 2017 begon ze daarnaast als externe promovenda aan de Radboud Universiteit Nijmegen onder leiding van prof. dr. Marlies Hulscher (Radboudumc) en prof. dr. Rob Ruiter (Universiteit Maastricht) en onder directe begeleiding van dr. Jeannine Hautvast en dr. Helma Ruijs. De resultaten van dit onderzoek zijn beschreven in dit proefschrift.

Naast haar opleiding Klinische gezondheidswetenschappen en haar promotie, was Anne werkzaam als verpleegkundige Maatschappij & Gezondheid bij GGD Gelderland-Zuid in de werkvelden jeugdgezondheidszorg, reisadvies en vaccinaties, en infectieziektebestrijding. Daarnaast was ze werkzaam als kwaliteitsmedewerker op de afdeling Algemene Gezondheidszorg. Sinds 2020 werkt ze als projectleider bij GGD GHOR Nederland bij team Gezondheid, waar ze sinds 2023 werkt bij het programma Versterking Infectieziektebestrijding en Pandemische paraatheid GGD'en.

Anne woont in Wijchen en is getrouwd met Wouter de Munter.

List of publications

Erik de Laat, **Anne C. de Munter**, Monica J. van der Burg, Dietmar J. Ulrich, Oliver J. Kloeters. (2017) A cross-sectional study on self-management of pressure ulcer prevention in paraplegic patients. Tissue Viability. Feb;26(1):69-74.

Anne C. de Munter, Alma Tostmann, Susan J.M. Hahne, D. Henri Spaan, Rijk van Ginkel, Wilhelmina L.M. Ruijs. (2018) Risk factors for persisting measles susceptibility: a case-control study among unvaccinated orthodox Protestants. European Journal of Public Health. Oct 1;28(5):922-927.

Anne C. de Munter, Wilhelmina L.M. Ruijs, Robert A.C. Ruiter, Dagmar J.J. van Nimwegen, Anke J.M. Oerlemans, Rijk van Ginkel, Marlies E.J.L. Hulscher, Jeannine L.A. Hautvast. (2020) Decision-making on maternal pertussis vaccination among women in a vaccine-hesitant religious group: Stages and needs. PLoS One. Nov 12;15(11):e0242261.

Anne C.de Munter, Tessa Schurink-van 't Klooster, Alies van Lier, Reinier Akkermans, Hester de Melker, Wilhelmina L.M. Ruijs. (2021) Determinants of HPV-vaccination uptake and subgroups with a lower uptake in the Netherlands. BMC Public Health. Oct 12;21(1):1848.

Anne C. de Munter, Tessa Schurink-van 't Klooster. (2022) Ecologisch onderzoek naar subgroepen met een lage HPV-vaccinatiegraad. Infectieziekten Bulletin. Februari.

Anne C. de Munter, Jeannine L.A. Hautvast, Wilhelmina L.M. Ruijs, Henri D. Spaan, Marlies E.J.L. Hulscher, Robert A.C. Ruiter. (2022) Deciding about maternal pertussis vaccination: associations between intention, and needs and values in a vaccine-hesitant religious group. Vaccine. Aug 19;40(35):5213-5222.

Anne C. de Munter, Jeannine L.A. Hautvast, Wilhelmina L.M. Ruijs, Robert A.C. Ruiter, Marlies E.J.L. Hulscher. (2023) Considerable doubt about rubella screening and vaccination among unvaccinated orthodox Protestant women: a mixed-methods study. BMC Public Health. Apr 14;23(1):693.

Research data management

The data presented in this thesis and collection during this PhD project at the Department of Primary and Community Care of the Radboud university medical center was archived according to Findable, Accessible, Interoperable, and Reusable (FAIR) principles.

Ethics

This thesis is based on the results of human studies, which were conducted in accordance with the principles of the Declaration of Helsinki. The medical and ethical review board Committee on Research Involving Human Subjects Region Arnhem-Nijmegen, the Netherlands concluded the studies were not subjected to Medical Research involving Human Subjects Act (WMO) and granted their approval [Reference nos.: 2014/1519 (Chapter 3); 2017/3178 (Chapter 4 and 5); 2018/4680 (Chapter 4 and 6); 2018/4744 (Chapter 2)]. The research in this thesis was supported by the research fund of the Dutch National Institute for Public Health and the Environment (RIVM), the Netherlands, for strengthening infectious disease control by local Public Health Services.

Study participants who participated in interviews and online focus groups (Chapter 4 and 5) filled in an informed consent form on paper. The paper informed consent forms were stored in a closed research locker of the department (Radboudumc, room M237, closet number 3.70) during the study. Online survey participants completed their informed consent digitally by accepting the link to the questionnaire (Chapter 3, 4 and 6).

Secured data storage

The project and data for the analysis of the studies of Chapter 3-6 are stored on the server of the Department of Primary and Community Care of the Radboud university medical center, department server: (H:)ELGdata$(\\UMCFS076) under \OZ-Public Health\REFO-VAC. Participant data used for the analyses of the study of Chapter 2 is stored on the National Institute for Public Health and the Environment (RIVM), department server: (R:)EPI\HPV\Opkomst under HPV vaccinatiegraad 2009 tm 2016. Data is accessible to authorized researchers of the research groups.

The privacy of the participants in the studies is warranted by use of encrypted and unique individual subject codes. Participant data traceable to individuals (Chapter 3-5) is stored separately from the study data on the server of the Department of Primary and Community Care of the Radboud university medical center: (H:)ELGdata$(\\ UMCFS076) under \OZ-Sleutelbestanden\VAC-refo.

Within two months after the defence of this thesis all research documents will be archived digitally conform the standard operating procedures of the Department of Primary and Community Care.

Following the guidelines of the Department of Primary and Community Care documents containing participant identifying data are archived separately from other study documentation and data. Study documentation and data will be saved for 15 years after termination of the studies.

Interoperability and Reusability

Written transcripts used in these studies are saved as .docx files. Qualitative data is imported in Atlas.ti, saved as .atlcb and .hpr7 files. Survey data were converged from LimeSurvey to Excel and IBM SPSS Statistics. Raw data of Chapter 2, 3 (anonymised data), 4 and 6 are stored in original form as .xlsx files.

Using these participant data in future research is only possible after a renewed permission by the participant as recorded in the informed consent. The datasets analysed during these studies are available from the corresponding author on reasonable request.

PhD portfolio

Institute for Health Sciences
Radboudumc

Name PhD candidate: **AC de Munter-Mulder**

Department: **Primary and Community Care**
Graduate School: **Radboud Institute for Health Sciences**
PhD period: **01-02-2017 – 01-12-2022**
Promotor(s): **Prof. dr. Marlies E.J.L. Hulscher, Prof. dr. Robert A.C. Ruiter**
Copromotor(s): **Dr. Jeannine L.A. Hautvast, Dr. Wilhelmina L.M. Ruijs**

Training activities	Hours
Courses	
- Kwalitatief interviewen (2017)	14.00
- Kwalitatieve analyse (2017)	14.00
- Multilevel analyse (2018)	28.00
- RU - Scientific Writing for PhD candidates (2019)	84.00
- RIHS - Introduction course for PhD candidates (2019)	15.00
- Radboudumc - Scientific integrity (2020)	20.00
- Proefschriftschrijfdriedaagse (2021)	35.00
- Radboudumc - eBROK course (for Radboudumc researchers working with human subjects) (2021)	26.00
- RU - Analytic Storytelling (2021)	28.00
Seminars	
- AMPHI tele-arena (2016) (oral presentation)	8.00
- AMPHI Arena (2017)	4.00
- Symposium Infectieziekte en Zwangerschap (2017) (oral presentation)	14.00
- AMPHI tele-arena (2017)	3.00
- AMPHI tele-arena (2018)	4.00
- ELG Onderzoekssymposium (2018) (oral presentation)	12.00
- ELG refereerbijeenkomsten (2018)	1.50
- AMPHI Tele refereren (2019)	1.00
- AMPHI tele-arena (2019) (oral presentation)	8.00
- AMPHI Arena (2019) (oral presentation)	10.00
- ELG Onderzoekssymposium (2019) (oral presentation)	3.00
- AMPHI tele-arena (2019)	4.00
- Webinar refereerbijeenkomst (2019)	2.00
- ELG refereerbijeenkomsten (2019)	1.50
- Vaccinology Masterclass (2020)	7.00
- AMPHI tele-arena (2020)	2.00
- KNAW-webinar: infectious disease epidemiology and the COVID-19 pandemic (2021)	1.50
- Masterclass online presentation (2021)	1.50
- Coronagedragunit: Vaccinatie (2021)	4.00
- AMPHI Arena (2022) (oral presentation)	10.00

Training activities	Hours
Conferences	
- Studiedag Dutch Biblebelt Network (2016) (poster presentation)	14.00
- Science Day Infectious Disease (2016) (oral presentation)	20.00
- ESCAIDE (2016) (poster presentation)	28.00
- Transmissiedag (2017) (poster and oral presentation)	21.00
- Studiedag Dutch Biblebelt Network (2017) (poster presentation)	8.00
- RVP Onderzoeksdag (2017)	7.00
- Science Day Infectious Disease (2017)	8.00
- Studiedag Dutch Biblebelt Network (2018) (poster presentation)	20.00
- Science Day Infectious Disease (2018) (oral presentation)	20.00
- RVP Onderzoeksdag (2019)	7.00
- V&VN Symposium: Vaccination (2019) (oral presentation)	14.00
- Studiedag Dutch Biblebelt Network (2019)	7.00
- Science Day Infectious Disease (2019)	7.00
- ESCAIDE (2020) (poster presentation)	21.00
- Studiedag Dutch Biblebelt Network (2021) (oral presentation)	20.00
- Studiedag Dutch Biblebelt Network (2021)	7.00
- ESCAIDE (2022) (poster presentations)	32.00
Other	
- Review scientific paper (2018)	6.00
- Review scientific paper (2021)	4.00
- Online presentation REC-RAC minisymposium (2022) (oral presentation)	6.00
Teaching activities	
Lecturing	
- Masterclass: Verpleegkundigen en onderzoek (2018)	8.00
Supervision of internships / other	
- Supervision Master student (2017)	56.00
- Supervision Literature Thesis Master (2019)	28.00
- Supervision Literature Thesis Master (2020)	28.00
- Supervision Literature Thesis Master (2022)	28.00
Total	**791.00**

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