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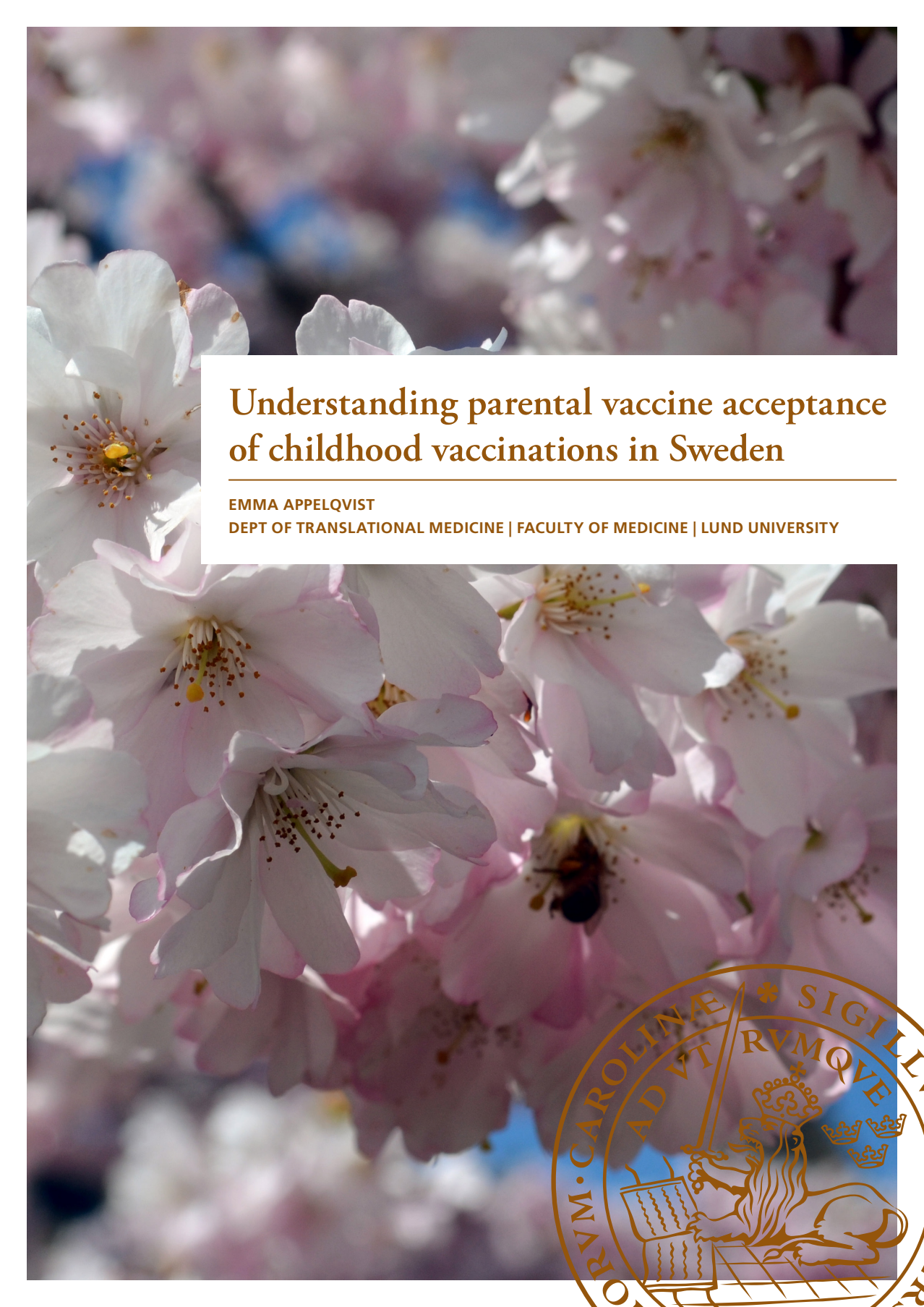
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Understanding parental vaccine acceptance of childhood vaccinations in Sweden

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Understanding parental vaccine acceptance of childhood vaccinations in Sweden

Emma Appelqvist



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DOCTORAL DISSERTATION

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Abstract: The vaccination coverage in Sweden's National Immunization Program (NIP) has been high and stable for decades. Although the coverage is high, few studies have assessed parental vaccine acceptance in Sweden. This doctoral thesis aimed to provide an in-depth understanding of current parental vaccine acceptance, focusing particularly on Human papillomavirus (HPV) and measles, mumps and rubella (MMR) vaccinations to further identify factors influencing low vaccine acceptance and to evaluate a tailored intervention to improve vaccine uptake. The purpose of the studies was to develop evidence-based methods to systematically inform the management and implementation of the NIP in Sweden regarding parental vaccine acceptance. Mixed methods were used to assess parental vaccine acceptance, including a survey and focus group discussions. A retrospective registry-based study, which included nearly 500,000 girls born from 2002 to 2010, examined factors for non-timely HPV vaccination and their respective parents. MMR vaccination was in focus for designing and implementing a tailored intervention based on the Tailoring Immunization Programs (TIP) approach targeting nurses working in an area with low MMR uptake. To evaluate, in-depth interviews were conducted with the nurses. The findings of the studies identified driving factors and barriers to parental vaccine acceptance. The majority of parents (79%) vaccinated their child without any doubts while others (19%) vaccinated their child but had questions or concerns and a small group declined at least one vaccination for their child (2%). Parents had confidence in vaccinations as they perceived them as safe and effective and trusted the system and nurses implementing the NIP. Individual and societal factors were driving factors as children were vaccinated for solidarity reasons and not only to get individual protection. Challenges and barriers identified related to safety concerns of adverse events or perceptions of negative or inadequate information. Nurses had a key role in the high parental vaccine acceptance. They provided a backbone for the NIP. The TIP approach provided a valuable, stepwise process that facilitated the identification and design of a tailored intervention targeting nurses. According to the nurses, the dialogue with parents having low MMR vaccine acceptance, was facilitated and enhanced following the tailored intervention. The TIP approach can be useful in addressing vaccination barriers and tailoring NIP to support an equitable and resilient program. Not being HPV vaccinated, according to the NIP in grades 5 and 6, was associated with parents having low or medium income or high school education as their highest education. Girls to parents where one was born abroad and the other in Sweden were also associated with not being vaccinated, regardless of whether the girl was born in Sweden or abroad. To conclude, the driving factors and barriers identified in the studies of this thesis provide an in-depth understanding of the current parental of vaccine acceptance. The driving factors can be promoted, and barriers can be addressed to strengthen the NIP. Systematic assessment of parental vaccine acceptance and inequity is valuable to inform the NIP implementation and to maintain high vaccination coverage in the future.

Key words: vaccine acceptance, childhood vaccinations, national immunization program, HPV vaccination, MMR vaccination, Tailoring Immunization Programs, inequity

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MADE IN SWEDEN 

To my family

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Populärvetenskaplig sammanfattning

Bakgrund

Vaccination är en av de viktigaste folkhälsoinsatserna för att rädda liv och hindra spridning av smittsamma sjukdomar. Tack vare vaccinationer har miljontals liv räddats världen över. Men det räcker inte att säkra och effektiva vacciner tas fram och tillgängliggörs. En förutsättning för framgångarna är att individer accepterar att bli vaccinerade. Under senare tid har forskningsområdet om vaccinacceptans hamnat allt mer i rampljuset då minskad acceptans för vaccinationer lyfts som ett hot mot framgångsrika vaccinationsprogram i världen. Vaccinacceptans handlar om individers och grupperns inställning till vaccination vilken kan förändras över tid och i olika sammanhang. Förenklat kan vaccinacceptans beskrivas som ett spektrum av inställningar till vaccination, från de som accepterar alla, de som accepterar men har betänkligheter eller funderingar kring vaccinationen, till de som skjuter upp eller avstår helt från vissa eller samtliga vaccinationer. Vaccinacceptans är komplext och individers inställning påverkas av vetenskapliga, psykologiska, kulturella, ekonomiska och politiska faktorer. Inte bara attityder, beteende och kunskap påverkar utan även strukturella och praktiska aspekter.

I Sverige erbjuds alla barn vaccinationer kostnadsfritt genom det nationella barnvaccinationsprogrammet. Vaccination sker på barnvårdscentraler (BVC) eller inom skolan beroende på barnets ålder. I flera årtionden har mer än 97% av alla 2-åriga barn i Sverige vaccinerats mot difteri, stelkramp, kikhosta och polio enligt barnvaccinationsprogrammet. Vaccinationstäckningen i Sverige är enastående hög internationellt sett. För att den höga vaccinationstäckningen ska bibehållas behöver vaccinacceptansen också fortsättningsvis vara god.

Vad är det då som gör att så många föräldrar i Sverige väljer att vaccinera sina barn? Hur resonerar föräldrar kring erbjudanden om att vaccinera sitt barn? Kunskap om föräldrars perspektiv och inställning till barnvaccinationer samt ökad förståelse om bakomliggande faktorer till föräldrarnas val är viktigt för att fortsatt främja acceptans av vaccinationer.

Syfte

Denna avhandling syftar till att få en djupare förståelse kring vaccinacceptans bland föräldrar i Sverige avseende vaccinationer i det svenska barnvaccinationsprogrammet. Studierna i avhandlingen ger underlag för det fortsatta arbetet med barnvaccinationsprogrammet i Sverige kring faktorer som påverkar vaccinacceptans. Särskilt fokus är på vaccination mot humant papillomvirus (HPV) och mässling, röda hund och påssjuka (MPR), för att beskriva faktorer bakom lägre vaccinacceptans och utvärdera en riktad insats för ökad vaccinationstäckning.

Metod

Fem studier genomfördes för att nå avhandlingens syfte. För dessa studier har både kvantitativ och kvalitativ metodik tillämpats. En enkätstudie (studie I) och en studie med fokusgrupper (studie II) genomfördes med föräldrar som målgrupp med huvudfokus på deras inställning till vaccinationer i barnvaccinationsprogrammet. Kopplat till vaccinationsprogrammet genomfördes även en registerstudie (studie III) med nära 500 000 flickor födda 2002 till 2010 med fokus på föräldrar till flickor som inte vaccinerats mot HPV i årskurs 5-6 i skolan enligt barnvaccinationsprogrammet. I ett försök att höja vaccinationstäckningen för MPR vaccination i ett område utanför Stockholm med lägre vaccinationstäckning togs en riktad insats för BVC-sköterskor fram (studie IV) och implementerades enligt Världshälsorganisationens TIP-metod, Tailoring Immunization Programs. Som utvärdering av den riktade insatsen genomfördes djupintervjuer med BVC-sköterskorna (studie V).

Resultat

Sammantaget visar studierna att föräldrars vaccinacceptans är komplex och påverkas av olika faktorer. En majoritet av föräldrarna i Sverige vaccinerade sina barn utan tvekan (79%) medan nära en femtedel (19%) av föräldrarna som vaccinerade sina barn hade frågor eller funderingar. En liten andel föräldrar (2%) valde att avstå att låta vaccinera sina barn med minst en vaccination. Faktorer som främjar en hög vaccinacceptans finns på både individ- och samhällsnivå. Föräldrar lät vaccinera sina barn både av individuella och solidariska skäl, samt värnade om värdet av barnvaccinationer. Det konstaterades att de sjuksköterskor, som utförde vaccination på BVC och i skolan, hade en nyckelroll för den höga vaccinacceptansen. Föräldrarna kände sig trygga med ett lyhört bemötande hos BVC-sköterskor och tilliten som byggdes under BVC-åren blev en grund hos föräldrarna för fortsatta beslut då barnet blir äldre. De faktorer som huvudsakligen var utmaningar för föräldrars vaccinacceptans var främst relaterade till funderingar om biverkningar och upplevelser av otillräcklig eller negativ information om vaccinationer. Spektrumet av informationsbehov hos föräldrar, oavsett vaccinationsbeslut, var stort och en utmaning som behöver adresseras. Dessutom förändras informationsbehovet när barnen blir äldre.

När riktade insatser behövs för att motverka låg vaccinationstäckning kan TIP-metoden som användes i studie IV och V vara ett lämpligt verktyg. Efter att den anpassade insatsen med seminarier, film och ett informationskort implementerats upplevde BVC-sköterskorna en förbättrad dialog med föräldrar som hade lägre acceptans för MPR vaccination. BVC-sköterskorna upplevde både ökat självförtroende att bemöta föräldrars frågor och funderingar samt att verktygen i insatsen var hjälpsam för att minska språkbarriärer.

Vaccination mot HPV har erbjudits kostnadsfritt som del i barnvaccinationsprogrammet sedan 2012. Trots detta identifierade en av studierna skillnader kring vilka som inte blev vaccinerade mot HPV. Av de flickor som ingick i studien hade 86% vaccinerat sig med minst en dos medan 14% var ovaccinerade vid slutet av årskurs 6. Studien visade att flickor vars föräldrar hade låg eller medelhög disponibel familjeinkomst och en gymnasieutbildning som högsta utbildningsnivå var i högre grad ovaccinerade mot HPV. Flickor födda 2003 och 2004 var ovaccinerade i större utsträckning än flickor med födelseår 2006 till 2010, men de socioekonomiska skillnaderna bestod även det sista studieåret, 2010. Vidare konstaterades att flickor med en förälder född i Sverige och en utomlands var ovaccinerade i större utsträckning, oavsett om flickan var född i Sverige eller utomlands. Även flickor födda i Sverige med föräldrar födda utomlands var ovaccinerade i större utsträckning än flickor födda i Sverige med båda föräldrar födda i Sverige. Flickor som inte blivit vaccinerade enligt barnvaccinationsprogrammet i årskurs 6, fick möjlighet till en försenad vaccination i årskurs 7 till 9, men även här bestod de socioekonomiska skillnaderna i vilka som fick en försenad HPV vaccination i grundskolan.

Slutsats

Baserat på den ökade förståelsen om föräldrars vaccinacceptans kan positiva faktorer för vaccination främjas och hindrande faktorer adresseras. TIP-metoden kan vara värdefull för att adressera hinder för vaccination och för att utveckla barnvaccinationsprogrammet till ett mer jämlikt och hållbart program. Återkommande undersökningar om föräldrars vaccinacceptans och analyser kring jämlikhet av vaccinationstäckningen är viktiga för att ge fortsatta underlag till barnvaccinationsprogrammet samt insatser för att bibehålla hög vaccinations-täckning i framtiden.

List of Papers

Paper I

Byström E., Lindstrand A., Bergström J., Riesbeck K. and Roth A. (2020) Confidence in the National Immunization Program among parents in Sweden 2016 – A cross-sectional survey. *Vaccine*. 2020;38(22):3909-17.

Paper II

Appelqvist E., Danielsson M., Jama A., Ask L. S., Stenhammar C., Lindstrand A., Riesbeck K. and Roth A. (2023). Parental views and the key role of nurses for high vaccine acceptance in Sweden - a focus group study. *BMC public health*, 23(1), 1786.

Paper III

Appelqvist E*, Löf E*, Kühlmann-Berenzon S., Lepp T., Sparén P., Lindstrand A., Riesbeck K., and Roth A. Determinants of non-timely HPV vaccination in the Swedish National Immunization Program for girls in compulsory school, 2013-2023 (manuscript).

*Shared first author

Paper IV

Jama A*, **Appelqvist E***, Kulane A., Karregård S., Rubin J., Nejat S., Habersaat K. B., Jackson C., Butler R., Lindstrand A. and Godoy-Ramirez K. (2022). Design and implementation of tailored intervention to increase vaccine acceptance in a Somali community in Stockholm, Sweden - based on the Tailoring Immunization Programmes approach. *Public Health in Practice*, 4, 100305.

*Shared first author

Paper V

Appelqvist E., Jama A., Kulane A., Roth A., Lindstrand A. and Godoy-Ramirez K. (2023). Exploring nurses' experiences of a tailored intervention to increase MMR vaccine acceptance in a Somali community in Stockholm, Sweden: a qualitative interview study. *BMJ open*, 13(2), e067169.

Abbreviations

BCW	Behavior Change Wheel
CHC	Child health care centers
CI	Confidence interval
COM-B	Capability, Opportunity, Motivation-Behavior
DTP	Diphtheria, tetanus, pertussis
FGD	Focus group discussions
HPV	Human papillomavirus
LISA	Longitudinal integration database for health insurance and labour market studies
MMR	Measles, mumps, rubella
NIP	National Immunization Programs
NVR	National Vaccination Register
OR	Odds ratio
PHAS	Public Health Agency of Sweden
PIN	Personal identification number
SAGE	Strategic Advisory Group of Experts at WHO
SCB	Statistics Sweden
STPR	Swedish Total Population Register
TIP	Tailoring Immunization Programs
VPD	Vaccine preventable diseases
WHO	World health organization

Preface

Ever since I discovered the field of public health and epidemiology during my bachelor's degree at Bates College, it has been of great interest to me. At the end of my master's program at Lund University I was looking for a project relating to vaccine preventable diseases or vaccinations for my thesis. I got a positive response from the Swedish Institute for Infectious Disease Control saying they were starting a project to pilot the Tailoring Immunization Programs approach where a master's thesis could contribute to the project. I was really disappointed when I realized it was a qualitative study they proposed, as I only had my mind set on doing a quantitative study assessing "real" numbers. Qualitative methods and "fluffy" interviews did not seem to be my thing at the time, but the topic seemed too interesting to let the opportunity go by. Little did I know that my qualitative study of views on vaccination among parents living in an anthroposophic community would spark a genuine interest in the field of vaccine acceptance and take me on a far greater journey for many years to come.

Context of this thesis

This thesis was carried out at the Public Health Agency of Sweden (PHAS) in collaboration with the Department of Translational Medicine, Lund University. In 2016, the research field of vaccine acceptance was starting to boom and with my interest in the topic, I suggested for my supervisors to make a PhD project focusing on parental vaccine acceptance from the perspective of the national immunization program in Sweden. We designed a research proposal that would be of value and support for the work of the vaccination program at PHAS while also contributing to my learning and development as a PhD student and researcher. Luckily, I started as a part-time PhD student at Lund University in the spring of 2017. The PHAS has funded my research with guidance and support from Lund University. While conducting my research part-time, I have also been working with the national epidemiological surveillance of pertussis, influenza, and COVID-19 and have been involved in the pandemic response. This thesis is a stepping stone and starting point for understanding and assessing parental vaccine acceptance in Sweden. I hope my thesis provides a foundation for future research to continue to understand parental vaccine acceptance in Sweden and inform the national immunization program.

Introduction

Ever since Edward Jenner developed the first vaccine against smallpox in 1796, the field of vaccinations has greatly impacted public health. One of the most incredible achievements in public health was the eradication of smallpox in 1980 following a successful global eradication program. Aside from clean drinking water, vaccinations are one, if not the most important, public health interventions to prevent morbidity and to save lives across the globe (1). Vaccinations save more than 4,4 million lives globally each year (2, 3) and more than 53 million lives are estimated to be saved by the measles vaccine alone from 2000 to 2022 (4). The success of vaccines for public health and populations worldwide is tied to the fact that individuals have accepted to get vaccinated with the vaccines.

Individuals having concerns about vaccinations or even being opposed to or anti-vaccination is not a new phenomenon, it has been around ever since the smallpox vaccine was developed and introduced (5-8). Vaccine critics have always debated vaccinations and along with the digital era with new ways of communicating and disseminating information, vaccine acceptance is on the radar more than ever, as lack of vaccine acceptance is a potential threat to the success of vaccinations. The best possible vaccines that science can produce will not have any public health impact if it is not accepted. The following quote illustrates the key factor of vaccine acceptance for public health;

“Vaccines don’t save lives. Vaccinations save lives”

Walter Orenstein

Vaccine acceptance and barriers to vaccinations

The success of vaccination programs may be threatened by changing or declining vaccine acceptance. The threat of declining vaccine acceptance came increasingly in the spotlight as a growing number of studies and reports had focused on vaccine hesitancy and vaccine acceptance (9-12). A striking increase in the number of published articles on the topic from 2007-2012 was noted in a global review (13). In addition, the paradox of vaccinations being victims of their own success fuelled, the interest in vaccine hesitancy even further as vaccine preventable diseases

(VPDs) became more rare and the focus shifted to potential adverse events and negative aspects of vaccinations. Mainly, as a resurgence of measles, including outbreaks in the US and Europe, was linked to vaccine hesitancy and refusal, the importance of the field was emphasized (14, 15).

During the same period, the channels for information and dissemination have developed and grown drastically with the internet and web 2.0, including social media, providing new ways of accessing information and sharing knowledge, not the least regarding vaccinations (16). The new digital platforms can facilitate the diffusion of accurate information regarding vaccination, as well as misinformation and critical anti-vaccination messages (16, 17). This also includes challenges to vaccine acceptance which can be even further enhanced or fuelled by the potential for polarization by the algorithms of social media, where messages, views and convictions may grow and flourish within certain settings. Examples have been seen where the vaccination debate has been influenced by misinformation messages spread on Facebook, YouTube, and Twitter (18-20). Another relevant and related aspect is the patterns of stigmatization as the focus on vaccine hesitancy has sparked a dichotomous view and discussions where individuals were perceived to be either pro-vaccines or anti-vaccines.

As the topic of vaccine hesitancy and acceptance received more attention, public health organizations and the World Health Organization (WHO) increasingly engaged and brought the discussions to higher policy-maker levels. The media also started to highlight vaccine hesitancy frequently in various ways. In 2019, the WHO listed vaccine hesitancy as one of the top 10 threats to global health, alongside air pollution, climate change, and antimicrobial resistance (21). A lack of confidence or increased hesitancy was seen to potentially hamper the success of vaccination programs for VPDs globally. In 2014, the WHO Strategic Advisory Group of Experts (SAGE) defined hesitancy as (22, 23):

“delay in acceptance or refusal of vaccination despite availability to vaccination services. Vaccine hesitancy is complex and context specific, varying across time, place and vaccines. It is influenced by factors such as complacency, convenience and confidence.”

As the research field emerged, the term vaccine hesitancy has been used frequently and heterogeneously, and it has been applied slightly differently in various studies (23, 24). In addition, terminology in terms of attitudes, beliefs, and confidence in relation to vaccines or vaccination programs has been used frequently. The term vaccine acceptance has also been used to describe the extent to which individuals accept, question, or refuse vaccination (25). The definition has also been slightly refined to reflect the decisions to either accept or decline vaccination when offered an opportunity to vaccinate or the timely receipt of recommended vaccinations when available (6, 24, 26). The concepts of vaccine hesitancy and vaccine acceptance overlap and the terms have been used interchangeably. Vaccine acceptance and

hesitancy describe a heterogeneous group along a continuum spanning from individuals accepting all vaccinations without doubts to those refusing vaccinations without doubts (Figure 1)(23). Along this spectrum, hesitant individuals may accept some vaccinations while having questions and concerns or delay some vaccinations, not necessarily refusing all vaccinations. The aspect of vaccine demand is also interrelated and illustrated at each far end of the vaccine acceptance spectrum. The demand ranges from high demand to no demand (23). Even though vaccinations are accepted by parents, they might not actively demand vaccinations for their children. On the other hand, as acceptance decreases, the demand for vaccinations might be undermined. As the word hesitancy often has a dichotomous and slightly negative connotation, this thesis mainly uses the term vaccine acceptance.



Figure 1. An adapted version for this thesis of “the continuum of vaccine hesitancy” introduced by the SAGE Working Group on Vaccine Hesitancy
Source: MacDonald et al, 2015 (23)

Vaccine acceptance in Sweden

Knowledge and understanding of parental vaccine acceptance in Sweden has been limited. This section summarizes studies on parental vaccine acceptance in Sweden up until this PhD project was initiated. As the vaccine coverage and uptake for vaccinations in the National Immunization Program (NIP) has been high and stable, a need to further understand parental vaccine acceptance has not been stressed or emphasized. Only a limited number of cross-sectional studies relating to parental vaccine acceptance have been conducted occasionally and not systematically.

A couple of vaccine safety concern events have triggered studies and research to be conducted. Following a debate on the safety concerns regarding measles, mumps and rubella (MMR) vaccination in the 2000s, two studies in Sweden suggested that low vaccine acceptance was related to fear of adverse events or perceiving the vaccines as harmful, preference for natural immunity and perception of the VPDs being mild (27, 28).

In a European collaboration, the VACSATC study, a national survey was conducted on attitudes to vaccinations among parents of 2-year-old children in Sweden in 2009

(29). Generally, 88% of parents perceived vaccination for children as important, however, a proportion of parents had doubts (17%) about vaccinations or had been worried about the safety of the vaccination (8%). Nurses were the most used and trusted information source on vaccinations (29).

A government initiative was launched in 2013 for the National Board of Health and Welfare (S2013/240/FS) to inform the legislation and regulation for NIP (Folkhälsomyndigheten, Dnr 02407-2015). As part of this initiative, studies were conducted regarding vaccine acceptance among parents of children aged 0-16 years to inform a long-term communication strategy. Both focus group discussions (FGDs) and a survey were conducted. Prior to the studies, the influenza pandemic of “swine flu” had brought vaccinations into the spotlight as influenza vaccinations and cases of narcolepsy have frequently been discussed in national media and social media in Sweden. Following the discussions, concerns had been raised that the unforeseen adverse event of narcolepsy among children following influenza vaccinations during the “swine flu” pandemic 2009-2010 would potentially have had a negative influence on the NIP for children. Results showed, however, that the general vaccine acceptance and awareness of the NIP was still high, and nearly all, 95%, had vaccinated their child for the childhood vaccinations offered in NIP. Hence, the impact of the pandemic influenza vaccination on the vaccine acceptance of childhood vaccinations in the NIP was limited. Although some parents who vaccinated their children had questions and concerns, the primary reason not to vaccinate was fear of adverse events, parents trusted the health care system and national agencies as a source of information about childhood vaccination. Information directly provided by health care professionals was preferred.

Vaccination against Human papillomavirus (HPV) is one of the more recently introduced vaccinations in the NIP and therefore, more research has been conducted regarding vaccine acceptance for HPV. Studies on HPV vaccination for girls after the introduction of the NIP have revealed that parental decision-making regarding the vaccination of their girls is complex (30). Parents vaccinated their daughters as they felt responsible for protecting them against cancer (31). A facilitating factor for the parents was their trust in vaccination recommendations from the authorities (31). Parents accepting and declining vaccination have both requested additional information and voiced concerns that information has been insufficient for decision-making (30-32). Requests have also been made for dialogue with the vaccinating nurses in school in addition to written information provided (31). Barriers to HPV vaccination include the perception of parents that their daughters were too young to be vaccinated when offered according to the NIP and that vaccination could influence sexual behaviors negatively (30, 32). Although parents chose to vaccinate their children, safety concerns of HPV vaccination including the risk of adverse events have been expressed by parents (31).

Vaccine acceptance in Europe

Parental decision-making for vaccinations in high-income countries has been shown to be complex and multi-dimensional as several factors, including societal, cultural and psychological factors, may influence the process (33). A global-level survey identified risk-benefits, including vaccine safety concerns and adverse events, as the main reasons for vaccine hesitancy (34). As the research field emerged, surveys have been developed to identify parents having lower vaccine acceptance (35, 36). An initiative, “the Vaccine Confidence Project”, was launched to monitor vaccine confidence through global surveys over the years and to allow for comparisons across countries. In one of the studies, the European region was identified as having a higher level of vaccine safety concerns than other regions globally, as individuals, to a larger extent, disagreed on questions regarding vaccine safety (37). National initiatives of monitoring and tracking of attitudes over time were seen in the UK and quantitative and qualitative studies were also conducted on vaccine acceptance, for instance, in the Netherlands (38-41).

The main barriers and challenges identified for hesitancy and lower vaccine acceptance in Europe have related to safety concerns, including adverse events (42-45). Perceiving a low risk of getting the VPDs or low severity of the disease has also been highlighted to influence vaccine acceptance (42-44, 46, 47). The aspect of information is also vital for vaccine acceptance as parents perceiving inadequate or insufficient information about vaccinations have a tendency toward lower vaccine acceptance. Lack of adequate information regarding childhood vaccinations has been identified to influence vaccine acceptance, particularly in studies focusing on HPV and MMR vaccination (44-46). Moreover, parental trust in information has also been raised as an important factor for vaccine hesitancy and low vaccine acceptance (44, 46). Trust in health care systems and the health professionals providing vaccinations as well as trust in information have also been identified as important for vaccination decisions (29, 46, 48-50).

Examples of drops in vaccination coverage in Europe

There have been instances where a drastic drop in vaccination coverage have been seen on national levels due to concerns about vaccinations and decreased vaccine acceptance. In 1998, a study by Wakefield et al. was published linking autism to MMR vaccination, which sparked controversy (51). The study received widespread negative publicity and raised concerns about the vaccine among parents. The study turned out to be spurious, and the article was later retracted, but the concerns affected parents, and drops in coverage were seen in several countries in Europe, including the UK and Sweden. In the UK, the debate peaked in 2002. In Sweden, the MMR vaccination coverage dropped temporarily, coinciding with the debate on the MMR vaccine, but later, it recovered to previous levels of vaccination coverage.

Extensive international studies and reviews have been conducted, but no association between autism and MMR vaccines has been identified (52-54). More recently, Denmark and Ireland experienced drops in HPV vaccination coverage due to negative media reporting regarding the safety of the HPV vaccine and adverse events affecting previously healthy, vaccinated young girls. In 2015, a documentary regarding this was aired on national television in both countries which received a great deal of attention both in media and also in social media. In Denmark, the vaccination coverage for the first dose of HPV vaccination for girls born in 2002 and 2003 dropped from 90 to 54% (55). Similarly, in Ireland, concerns about the HPV vaccination were raised following the documentary and the debate in media and on social platforms was also fuelled by lobby groups (56). The uptake of the first dose of HPV vaccination in Ireland only reached 50% in 2016-2017, whereas a few years prior, the uptake was 80% for fully vaccinated girls (56). The European Medicines Agency reassessed the safety of the HPV vaccines at Denmark's request and their review declared the HPV vaccination to be safe (57). Impressively, dedicated and focused efforts with national interventions in both Denmark and Ireland reversed the trend of lower coverage for HPV (56, 58). The examples of declining confidence in the HPV vaccination and concerns for the vaccine in Europe had dramatic effects on the vaccination coverage at national levels. These experiences highlights that vaccination coverage may drop dramatically and quickly due to unfounded concerns receiving attention in public and social media, even in countries where vaccines have been implemented and vaccination coverage is high. Thus, vaccine acceptance and trust in vaccinations cannot be taken for granted, but continuous and active work is needed, even in countries with generally high vaccine uptake.

Frameworks for understanding vaccine acceptance

Vaccine acceptance is multi-factorial, complex, and context-dependent. Not only scientific evidence and facts are of importance but also cultural, political and societal factors as well as psychological factors and behaviors (8-10, 33). A multifaceted mix of factors for vaccine acceptance makes it challenging to comprehend and capture entirely. Factors influencing vaccine acceptance are, in reality, interrelated and overlapping, making it difficult to single out specific elements. Different frameworks have been developed to describe factors influencing vaccine acceptance to facilitate the understanding of vaccine acceptance as the research field has emerged and expanded. Only a few of the frameworks developed are highlighted below to showcase the complexity of factors influencing vaccine acceptance.

A “3 Cs” model for vaccine hesitancy was introduced in the literature to highlight factors influencing hesitancy (Figure 2)(23). The three “C”s stand for complacency, convenience and confidence. Confidence in vaccination is an essential concept and

for the 3C model, it has been defined as trust in “the effectiveness and safety of vaccines, trust in the system that delivers them as well as trust in the motivations of policy-makers who decide on the needed vaccines” (23). The concept of complacency relates to the perception of the risk of VPDs and the individual's perceived necessity and value of vaccination to prevent disease. The aspect of convenience relates to the contextual situation such as the availability of vaccinations, the perceived quality of health systems offering and delivering vaccinations, proximity to vaccination services and the cost, both actual monetary cost and cost in terms of time.

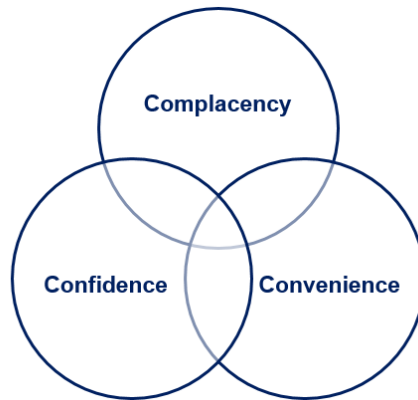


Figure 2. The “three Cs model”

Source: MacDonald et al, 2015 (23)

The 3Cs model has evolved over the years by researchers to include additional “Cs” including “calculation” and “collective responsibility” in a “5C” framework and, most recently, a “7C” framework also included “conspiracy” and “compliance” (59-61).

A vaccine hesitancy matrix has been proposed by the SAGE Working Group on Vaccine Hesitancy (Table 1) (13, 23). The model included three areas: contextual influences, individual and group influences, and specific issues related to vaccines and vaccinations.

Table 1. Determinants of the “vaccine hesitancy matrix” by the SAGE Working Group on Vaccine Hesitancy (23) .

Contextual influences	
Influences arising due to historic, socio-cultural, environmental, health systems/institutional, economical or political factors	<p>Communications and media environment</p> <p>Influential leaders, immunization program gatekeepers and anti- or pro-vaccination lobbies.</p> <p>Historical influences</p> <p>Religion/culture/gender/socio-economic</p> <p>Geographical barriers</p> <p>Perception of the pharmaceutical industry</p>
Individual and group influences	
Influences arising from personal perception of the vaccine or influences of the social/peer/environment	<p>Personal, family and/or community members experience with vaccinations, including pain.</p> <p>Beliefs, attitudes about health and prevention</p> <p>Knowledge/awareness</p> <p>Health system and providers-trust and personal experience.</p> <p>Risk/benefit (perception)</p> <p>Immunization as a social norm vs not needed/harmful</p>
Vaccine/vaccination-specific issues	
Directly related to vaccine or vaccination	<p>Risk/benefit (epidemiological and scientific evidence).</p> <p>Introduction of a new vaccine or new formulation or a new recommendation for an existing vaccine</p> <p>Mode of administration</p> <p>Design or vaccination program/Mode of delivery (e.g. routine vaccination or mass vaccination program)</p> <p>Reliability and/or source of supply of vaccine and/or vaccination equipment</p> <p>Vaccination schedule</p> <p>Costs</p> <p>The strength of the recommendation and/or knowledge base and/or attitude of healthcare worker</p>

More recently, a behavioral and social drivers (BeSD) framework has been developed by WHO to support the understanding of barriers and drivers for vaccination uptake (Figure 3). The framework includes aspects that could be modified to favor acceptance and thereby vaccine uptake. The factors include emotional, social, psychological, motivational and practical aspects (62).

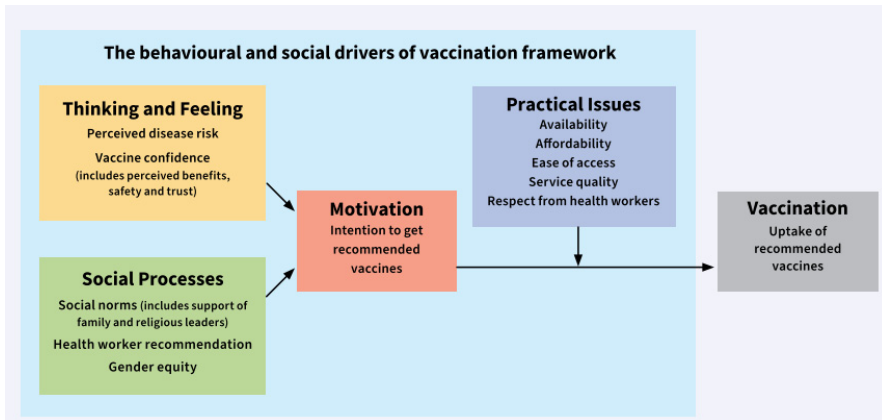


Figure 3. Overview of the behavioral and social drivers (BeSD) framework developed by WHO
Source: World Health Organization, 2022 (62)

A more general framework for health behaviors, COM-B (capability, opportunity, motivation – health behaviors) has been adapted for the field of vaccine acceptance by the WHO Regional Office for Europe to understand vaccination behaviors (Figure 4) (63-65). The COM-B model identifies factors relating to capability, opportunity, and motivation, which are three interlinked factors required for any health behaviors. The use of the model was motivated by including a broad range of factors. The capability and motivational factors reflect the individual level, whereas opportunity reflects the contextual aspects.

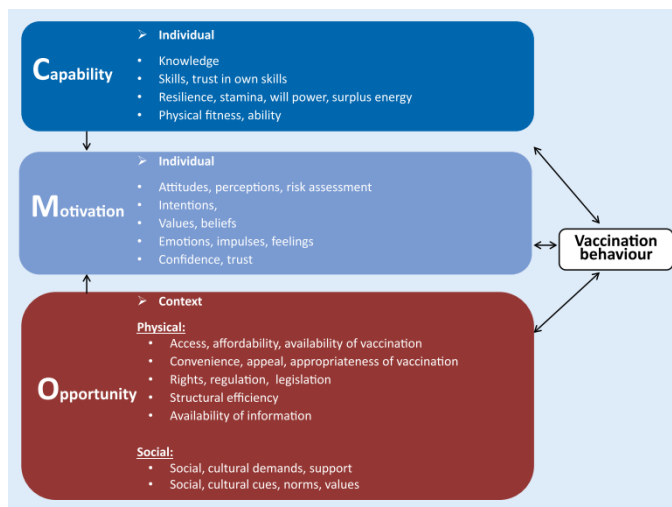


Figure 4. An overview of the adapted Capability, Opportunity, Motivation-Behavior (COM-B) model for vaccinations.

Source: Habersaat KB, Jackson C., 2019 (63).

Low vaccine uptake and inequity

Vaccine acceptance is not equivalent to vaccination coverage, and uptake and low or sub-optimal vaccine uptake cannot be attributed only to low vaccine acceptance. Vaccine uptake only reflects the proportion of a population getting vaccinated, and it should not be mistaken to reflect vaccine acceptance, as several other barriers may hamper the uptake (6). Assessment of lower vaccine uptake and coverage, however, can be a starting point for identifying immunization gaps and sub-groups and populations and for understanding the barriers behind the uptake. The SAGE working group on vaccine hesitancy suggested in 2014 that pockets and subgroups with sub-optimal coverage should be identified and further assessed routinely as part of good immunization program management (22). Immunization gaps with the accumulation of unvaccinated children, especially in marginalized populations, have highlighted the need to understand barriers further and also drivers for vaccinations to be able to support vaccinations for increased uptake (66-68). Vaccine acceptance is a piece of the puzzle, but a broad perspective on barriers and drivers should be considered, including vaccine acceptance along with other individual and contextual factors.

The vaccine uptake and coverage for MMR vaccinations in Europe in recent years along with the epidemiology of measles, makes an important point of the need to understand low vaccine uptake and barriers to MMR vaccination as the cases of measles have been on the rise (69). The re-emergence of measles is a public health concern and threatens the health of unvaccinated individuals. In the WHO European Region, an increase in measles was already seen from 2015 to 2019 as the number of reported cases increased from 5,000 cases to more than 160,000 cases and over 100 measles-related deaths between January 2018 to May 2019 (70, 71). In the following years, exceptionally few cases of measles (127 cases) were reported during 2020-2022, coinciding with the COVID-19 pandemic as countries implemented public health measures to limit the transmission of SARS-CoV-2 (69, 72). Thereafter, in 2023, an alarming resurgence of measles was observed in the European region as 30,000 cases were reported in 40 of the 53 countries, including 21,000 hospitalizations and 5 measles-related deaths (69, 73). In the EU/EEA countries, 2,361 cases of measles were reported in 2023 for which Austria and France reported outbreaks of measles, and Romania declared an epidemic of measles, which accounted for the majority of the cases (69). The majority of the cases were due to local transmission of measles.

During the COVID-19 pandemic, vaccination coverage in NIPs declined in the WHO European region. In 2020 and 2022, it has been estimated that more than 1.8 million infants did not receive a measles vaccination (73). Overall, the vaccination coverage for the first dose of measles vaccine dropped from 96% in 2019 to 93% in 2022 (69). Due to suboptimal vaccination coverage below the recommended threshold of 95% coverage for achieving herd immunity and prevention of

transmission (70, 71), there has been an accumulation of susceptible children and adults. The WHO has highlighted the significance of including vaccine acceptance as part of understanding vaccine uptake as they recommend monitoring behavioral and social drivers (BeSDs) on a routine basis in relation to vaccine uptake and addressing inequity in vaccination programs (74).

Inequity

From a NIP perspective, it is valuable to assess vaccine uptake in terms of equity and social determinants to identify potential barriers to vaccination from a different angle and understand how it possibly relates to vaccine acceptance or other factors. Achieving equitable vaccination programs has been stated as a priority in the European Vaccine Action Plan 2015–2020 (75). To ensure equitable access to immunizations, vaccination programs and services should be adapted and tailored to meet the needs of individuals (76). The imbalance that stems from systematic differences in health outcomes that can be avoided has been defined as health inequity (77). Social determinants are non-medical factors that influence the health of individuals, including the conditions in which people live and work (78, 79). Along a social gradient of health, individuals on the lower end of the social hierarchy have worse health than those on the higher ends of the hierarchy (79). The WHO suggests that analysis of inequalities in vaccination uptake should include four key determinants: socioeconomic status, geographical location, educational status of parents, ethnicity, and migration status (76).

Social determinants and low socioeconomic status have been associated with lower vaccine uptake of childhood immunizations (80, 81). HPV vaccination in Scandinavia is an illustrative case of inequities for vaccinations and the implications as research on HPV vaccination has linked social determinants to both the low HPV vaccination coverage and the incidence of cancers. Registry-based studies have shown that higher incidence and lower survival of cervical cancer relate to social determinants as the incidence of cervical cancer increased with lower social position (82). This is particularly alarming as social determinants have also been linked to lower uptake and non-vaccination for HPV. In Sweden, HPV non-vaccination has been associated with having an immigrant background and parents with low disposable family income as well as low education for girls born 2003-2008 (83). Similarly, girls having a mother with lower education, lower disposable income and being unemployed have been associated with lower initiation of the first dose of HPV vaccination in Denmark (84). Girls having an immigrant background have also been identified for lower uptake of HPV vaccination (first dose) in Denmark and for less completion of catch-up vaccination in Norway (85, 86). Interestingly, high education of mothers was associated with less initiation of HPV vaccination during the initial years of HPV implementation in the school-based program in Norway (87). Consequently, the inequities observed are of public health importance as the group of girls with a higher incidence of cervical cancer is particularly vulnerable

by not receiving HPV vaccinations. Additionally, HPV-vaccinated girls have been shown to be more likely to attend the screening for cervix cancer in Sweden than unvaccinated girls (88).

The Tailoring Immunization Programs approach

To address the inequities, identifying social determinants associated with lower uptake is not enough; further exploration of the barriers behind the factors associated with non-vaccination is needed. To support countries in achieving more equitable uptake, the “Tailoring Immunization Programmes” (TIP) approach was developed and launched in 2013 by the WHO Regional Office for Europe (89). The TIP approach aims to facilitate a deeper understanding of drivers and barriers for suboptimal vaccination coverage and provide a tool for addressing equitable vaccination uptake (64, 90). The approach guides the process from identifying populations and target groups with lower vaccination coverage to developing and implementing tailored, evidence-based interventions based on the findings of barriers and drivers (Figure 5) (64, 90). The TIP approach has been revised and further developed over the years based on evidence and country experience, including the contribution from the application experience in Sweden. The latest edition of the TIP approach also includes sections on monitoring and evaluation.

The TIP approach is based on scientific evidence from social and behavioral science research, and theoretical frameworks have been adapted to provide behavioral insights for vaccinations (63, 64, 89). Both the Capability-Opportunity-Motivation-Behavior (COM-B) model and the Behavior Change Wheel (BCW) framework provide a theoretical foundation for the TIP approach (63). Currently, the TIP approach has been used and implemented in more than 10 countries from 2013 to 2021, targeting different communities (91-100). Recently, a THP guide – “Tailoring Health Programs”, inspired by the TIP approach, was launched by the WHO (101).

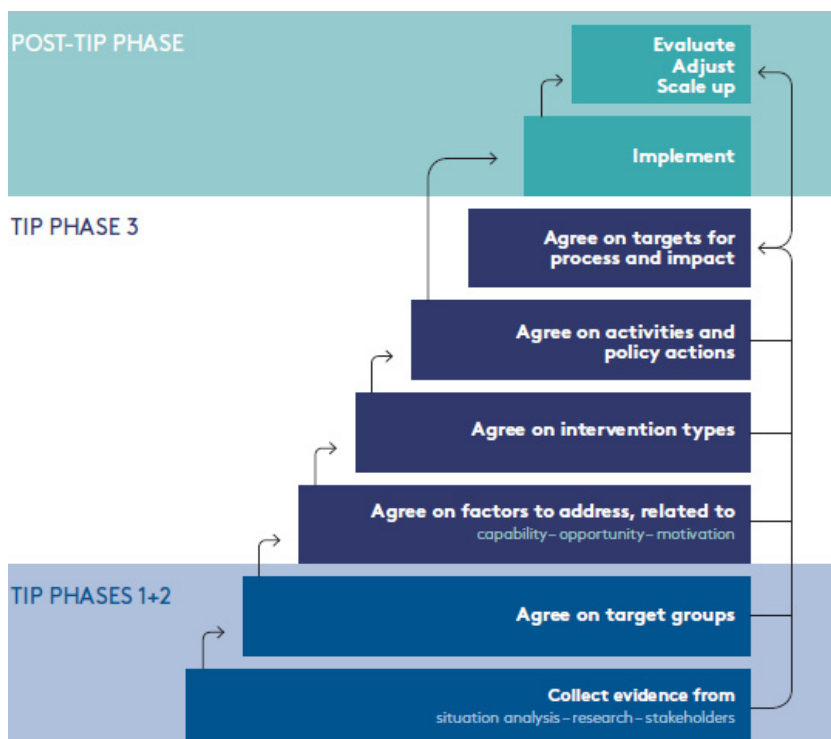


Figure 5. An overview of the tailoring immunization programs (TIP) phases for developing and implementing interventions.

Source: WHO Regional Office for Europe; 2019 (64)

The launch of TIP in Sweden

Sweden and the PHAS was one of the first countries to pilot and implement a TIP project in 2013 (based on the TIP approach version 1, 2013) (89). Initially, the project focused on formative research to understand barriers and drivers in communities with low MMR vaccine uptake or at risk of low MMR uptake. The districts of Rinkeby and Tensta north of Stockholm were identified to have low vaccination coverage for MMR vaccination for two-year-olds. The vaccination coverage started to decline in 2000 and had since stabilized at 70% coverage between 2002 and 2013. Thus, formative studies were conducted in a Somali community (102, 103). In addition, the TIP project also included studies with undocumented migrants (104) and in an anthroposophic community (105). The TIP project with focus on the Somali community will be further described in the coming chapters of this thesis.

Vaccinations and the National Immunization Program

MMR vaccination

Measles is one of the most contagious diseases. Infected individuals can transmit the morbillivirus virus by respiratory droplets and aerosols when sneezing and coughing (106). Airborne droplets may be present for up to two hours after an infected person has left a room. The secondary attack rate can be as high as 90%, for which one measles-infected person can infect 9 out of 10 unvaccinated individuals in their household or proximity (106). The incubation period is usually 10 to 12 days. Measles can cause severe and potentially life-threatening disease. About 20% of the cases get complications such as diarrhea or secondary bacterial infections, otitis media and pneumonia (107). In very rare cases (1 case per 10,000-100,000 cases of measles), a fatal disease develops, subacute sclerosing panencephalitis (SSPE), years after a measles infection (108, 109). Measles vaccination for children was introduced in Sweden in 1971 and changed in 1982 to a two-dose schedule for MMR vaccine (107, 110). The vaccine is a live attenuated vaccine. The vaccine effectiveness of one dose given at or after 12 months of age is estimated to be 93% and 97% for two doses of MMR vaccine (106, 111).

Elimination of measles

The WHO European region has since 2010 recommitted to eliminating endemic transmission of measles and also rubella (112). The aim of elimination has been highlighted in the European Action Plan 2015-2020 and, more recently, in the European Immunization Agenda 2030. At least 95% vaccination coverage for two doses of MMR vaccination needs to be achieved in the population for all age groups and population groups to reach the goal of elimination.

Epidemiology in Sweden

Measles is a notifiable disease according to the Communicable Disease Act in Sweden. Since the introduction of MMR vaccination in the NIP, the number of cases has decreased drastically. In 2015, the Regional Verification Committee of WHO declared measles to be eliminated in Sweden (113). In recent years, the vast majority of measles cases have either been imported or epidemiologically linked to an imported case. Only a few sporadic cases have had an unknown origin. In the past 20 years, the number of reported cases of measles per year has ranged from 0 to 51 cases (Figure 6) (114). In 2023, only 11 cases of measles were reported nationally (115). There are currently no indications of resurgence of measles in Sweden. One of the more recent outbreaks in 2017 involved cases in the Rinkeby and Tensta area outside Stockholm. The area has an increased risk of outbreaks due to an accumulation of susceptible individuals, mainly through low vaccine uptake. From

January to March 2017, 12 cases of measles were reported in the area, of which nine were children (116).

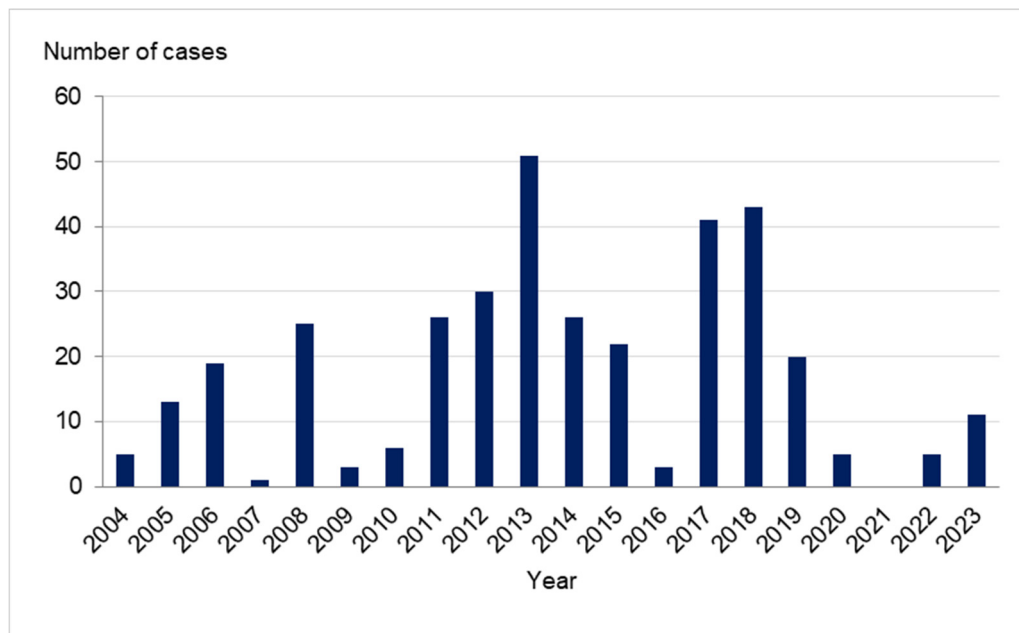


Figure 6. The number of reported cases of measles per year in Sweden, 2004-2023.
Source: Folkhälsomyndigheten (110, 115)

HPV vaccination

HPV causes infections in the reproductive tract and amongst young women it is the most common sexually transmitted infection. Globally, the prevalence is estimated to 22% amongst young women under the age of 25. Most (70-90%) infections are asymptomatic and resolve spontaneously within two years. Precancerous lesions, however, may develop due to persistent infection, which in turn may lead to cancer years later if the lesions are not detected and treated. HPV is known to cause cancers in the cervix, vulva, vagina, penis, anus and oropharynx (117). There are around 200 different strains of HPV of which HPV 16 and 18 have been found to be particularly carcinogenic and linked to cause 71% of cervical cancers (118). From a global perspective, cervical cancer is the fourth most common type of cancer for women with close to 600,000 cases and 300,000 deaths estimated annually to be due to cervical cancers (119). In Sweden, approximately 800 women and 300 men are diagnosed with HPV-related cancers each year. In 2021, 530 cases of cervical cancer were diagnosed in Sweden (120).

Vaccines against HPV became available in 2006. A bivalent vaccine (Cervarix™) protects against HPV 16 and 18 and a quadrivalent vaccine (Gardasil™) protects against HPV 6, 11, 16 and 18. Later, a 9-valent vaccine was approved, including protection against HPV 6, 11, 16, 18, 31, 33, 45, 52 and 58. A substantial reduction of HPV 16 and 18 as well as herd effect for boys and other age groups of women has been observed following the implementation of HPV vaccinations for girls in national programs (121, 122). Studies in Sweden have shown a reduction in genital warts (123-125) and HPV infections following HPV vaccination (126). More importantly, HPV vaccination has been shown to substantially reduce the risk of cervical cancer for women up to the age of 31 (127). The vaccines have over 90% protection against the HPV types that are included in the vaccines if vaccinated before exposure to HPV.

Implementation of HPV vaccination in Sweden

HPV vaccination has been implemented in Sweden by different modes and schedules over time (Figure 7). Initially, in 2007-2012, the vaccination was subsidized opportunistic for girls aged 13-17 years. For this mode of delivery, a vaccine uptake amongst the eligible group of girls was achieved by 37% (128). In January 2012, HPV vaccination was implemented in the Swedish NIP following a decision taken in 2010. By including HPV vaccination in the NIP, the vaccination was offered by a school-based program free of charge for girls in 5th grade (11-12 years) or 6th grade (12-13 years). Girls born in 1999 were the first cohort to be offered the vaccination. Initially, HPV vaccination was implemented as a three-dose schedule, but it was changed to a two-dose schedule in 2015 following a recommendation issued by WHO. Based on new evidence that a single dose of HPV vaccine has about the same effectiveness as 2 doses, the WHO currently recommends either 1 or 2 doses of HPV vaccine (118). Sweden has, however, not yet changed its policy for the NIP. The HPV vaccination is offered voluntarily, and the school health services require written consent from both guardians for the girl to be vaccinated. Since 2016, unvaccinated individuals can get vaccinated free of charge, according to the NIP, up until the age of 18. Alongside the implementation of HPV vaccination in the NIP in 2012, girls born 1993-1998 were offered free catch-up HPV vaccination, and the subsidy was also extended to include girls aged 18-26 years. Additionally, HPV vaccination was also offered free of charge to girls up to 26 years of age for a period of time in some regions. The vaccination coverage by mode of implementation is shown in Figure 8. Gender-neutral HPV vaccination was also implemented in the NIP to include boys born in 2009 and later in August 2020. Along with the implementation of the gender-neutral HPV vaccination, a policy change was made to the NIP schedule, for which HPV vaccination was only offered in grade 5 and not grades 5 to 6.

Elimination

In 2020, the WHO launched a Global Strategy to Accelerate the Elimination of Cervical Cancer. The elimination includes targets for screening, treatment and, most importantly, vaccination by 2030 (118, 119). The goal is to reach 90% of fully vaccinated 15-year-old girls. Over the coming decade, the initiative is estimated to prevent approximately 60 million cases of cervical cancer and also 45 million deaths (129, 130).



Figure 7. Timeline of the different modes of implementation for HPV vaccination for girls in Sweden by birth cohort.

Source: Wang et al, 2019 (128)

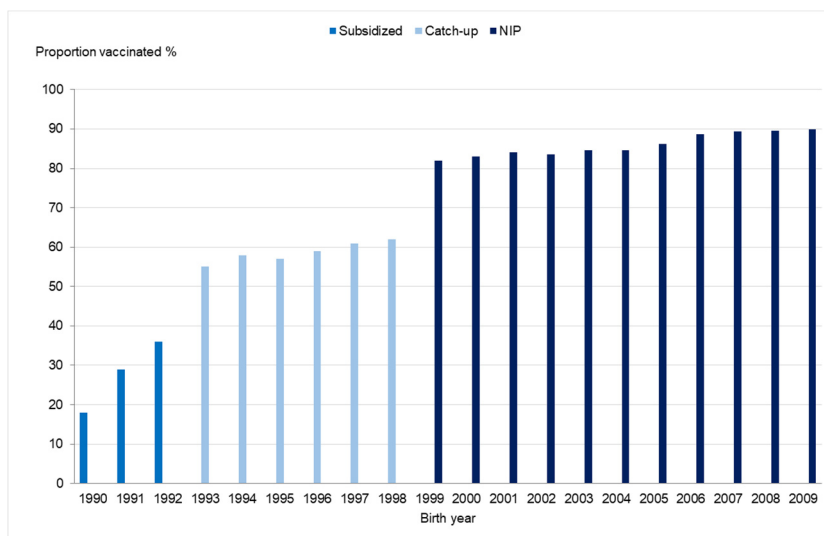


Figure 8. The proportion of girls vaccinated with at least one dose of HPV vaccination. Data for girls born 1990-2001 at the end of 2016 and data for girls born in 2002-2009 at the end of 2021.

Source: Folkhälsomyndigheten.

The National Immunization Program in Sweden

Vaccinations have significantly impacted disease prevention in Sweden as the vaccination coverage for the NIP has been high and stable for decades. It has been estimated that more than 1,5 million cases of pertussis, poliomyelitis, measles and mumps have been averted up until 2019 since the introduction of vaccinations in the NIP (131).

The PHAS is responsible for the NIP, according to the Communicable Disease Act (SFS 2004:168) (132). The law stipulates that program changes and additions must be assessed by three criteria and accounted for by 13 factors, of which one relates to vaccine acceptance (133). Based on recommendations made by PHAS, the Swedish government decides whether to include the suggested vaccination or not in the NIP. Regions and municipalities are obligated to implement vaccinations included in the NIP. A complex organization implements the vaccination program and involves several functions and capacities. Continuous work to support the implementation is needed, for which new insights are important. The PHAS monitors the NIP and supports health professionals in their implementation. The PHAS is also responsible for the national surveillance of VPDs. In addition to the NIP, the PHAS may also issue separate vaccination recommendations, such as influenza vaccinations. Those recommendations are neither legally binding to implement for regions and municipalities nor obliged to be offered free of charge.

In Sweden, the NIP is voluntary and free of charge to all children. Currently, the NIP includes vaccinations against 11 diseases: rotavirus, diphtheria, tetanus, pertussis (DTP), polio, Haemophilus influenzae type b (Hib), pneumococcal disease, measles, mumps, rubella, and HPV. Since 2016, vaccination against hepatitis B has been included in regional vaccination programs in all regions, thus all children are offered hepatitis B in a combined vaccine at 3, 5 and 12 months of age. In August 2020, the latest change was made to the NIP in which gender-neutral vaccination for HPV was introduced to also include boys born in 2009 or later. The NIP vaccinations are implemented at child health care centers (CHCs) and in the school health services. The current vaccination schedule is shown in Table 2 (134).

The CHCs are responsible for all children aged 5 years and younger and offer preventative check-up programs for children as well as support and advice about child health. Health checkups by physicians are also offered routinely as part of the preventative program. The centers are often led by a paediatric or district nurse (135). About 99% of the children in Sweden attend the services that reach all socioeconomic groups (135). During the first year of a child's life, a family is offered at least 9 general health checks, one of which is an at-home visit by the nurse when the baby is newborn (136). For the NIP, vaccinations are offered on 4 occasions during the first 12 months, followed by visits at 18 months and 5 years. Children who are not fully vaccinated according to the NIP schedule are offered vaccinations at subsequent visits. A family often visits the same nurse for health checkups,

allowing for a trustful relationship to be built. Due to the close contact between the CHC nurse and the family, only oral consent from at least one caregiver is required to vaccinate the child.

For children aged 6-17 years, the school health services are responsible for implementing the NIP. Children are offered vaccination on 4 occasions in grades 1-2, 5 (two doses) and 8-9. School is compulsory in Sweden until grade 9. School health nurses carry out vaccinations. In contrast to vaccinations offered at CHC, all caregivers have to sign a written consent to vaccinate their child in schools. For children not having received all NIP vaccinations, the school health services should offer vaccinations free of charge until the child is 18 years old (137). Children may get the possibility to decide on vaccination themselves as they age, as the Patient Act in Sweden (Patientlag (2014:821)) states that children's wishes should be increasingly considered in relation to their age and maturity, although no specific age is specified (138).



My son Arvid and his CHC nurse Linda Olin at his 12-month check-up.

Table 2. The current National Immunization Schedule in Sweden 2024 (110).

Vaccination offered against:	Child health care centers						School health services					
	6 weeks	3 months	5 months	12 months	18 months	5 years	Grade 1-2	Grade 5	Grade 8-9			
Rotavirus	Dose 1	Dose 2	Dose 3*									
Diphtheria		Dose 1	Dose 2	Dose 3		Dose 4			Dose 5			
Tetanus		Dose 1	Dose 2	Dose 3		Dose 4			Dose 5			
Pertussis		Dose 1	Dose 2	Dose 3		Dose 4			Dose 5			
Polio		Dose 1	Dose 2	Dose 3		Dose 4						
Haemophilus influenzae type b (Hib)		Dose 1	Dose 2	Dose 3								
Pneumococcal disease		Dose 1	Dose 2	Dose 3								
Measles, Mumps, Rubella					Dose 1		Dose 2					
Human papillomavirus (HPV)								Dose 1 & 2				

*Dose 3 only relevant for certain rotavirus vaccines.

Vaccination coverage for the National Immunization Program

Data for vaccination coverage

The national vaccination coverage for the NIP was based on an annual report for children 2 years of age by the local CHCs up until 2021. For children born in 2019 and later, the official statistics for the NIP is entirely based on the national vaccination registry. A national vaccination registry (NVR) was implemented on January 1st 2013, for which the reporting of childhood vaccination included in the NIP is mandatory by law.

Prior to the implementation of HPV vaccination in the NIP, vaccinations included for subsidized and catch-up opportunities were registered in the Svevac-registry. As the HPV vaccination was implemented in the NIP 2012, vaccinations were registered in Svevac during the first year and since 2013 the NVR has been used for HPV vaccinations given as part of NIP.

Vaccination coverage

The vaccination coverage for 3 doses of vaccines preventing DTP, and polio has been over 97% for nearly three decades (Figure 9). The vaccination coverage for at least one dose of MMR has been 95% or higher for children born in 2003 and later (Figure 10). In 2021, more than 97% of 2-year-old children were vaccinated according to their schedule (139).

The HPV vaccination coverage for girls born in 1999, as the first cohort being offered the vaccination as part of the NIP, reached about 80% for the 1st dose (140). In more recent years, the vaccination coverage for girls born in 2009 was 90% (dose 1) and 83% (dose 2), at the end of 2021 (110). Although the national vaccination coverage has been high and stable, the coverage at regional or local levels may vary between different regions in Sweden and there may also be pockets with considerably lower vaccination coverage in communities.

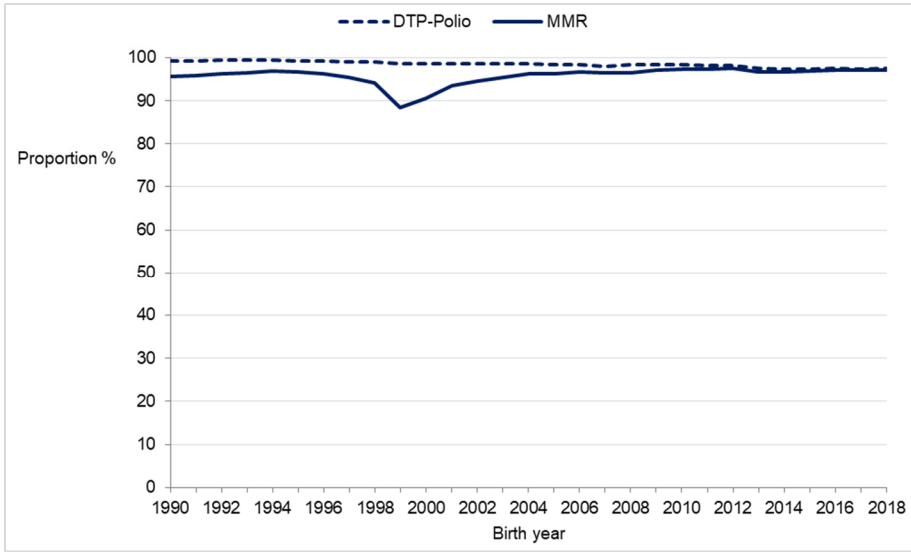


Figure 9. The vaccination coverage for children of 2 years of age in Sweden. Data is displayed for three doses of DTP-polio vaccine and one dose of MMR vaccine.

Source: Folkhälosmyndigheten

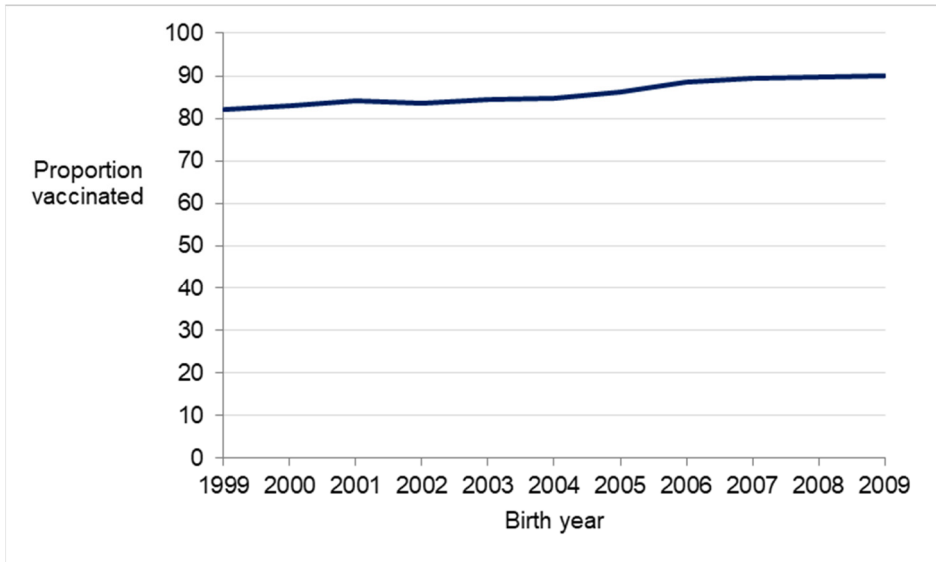


Figure 10. The vaccination coverage of at least one dose of HPV vaccination in the NIP for girls by birth year. Data for girls born 1999-2001 at the end of 2016 and data for girls born in 2002-2009 at the end of 2021.

Source: Folkhälsomyndigheten

Rationale

Even though the vaccination coverage for childhood vaccinations has been high and stable for decades in Sweden, factors for parental vaccine acceptance need to be understood to keep children protected against diseases. As the research field of vaccine acceptance has developed, it has highlighted the importance of assessing the driving factors and barriers for parental vaccine acceptance. This is highly relevant for the implementation of the NIP in Sweden to sustain vaccine acceptance in the future, as nearly all parents currently choose to vaccinate their children. The driving factors of vaccine acceptance are just as important to understand and to promote to build resilience in the NIP. The experiences of drops in HPV vaccination coverage in Denmark and Ireland due to safety concerns show that high acceptance cannot be taken for granted. Until now, only a limited number of studies have explored the vaccine acceptance of parents in Sweden for childhood vaccinations in the NIP. In addition, studies assessing inequity and determinants for non-timely vaccination of NIP vaccinations are also lacking. Identifying determinants for lower vaccine uptake and assessing inequities in vaccination programs is important to inform the management and implementation of the NIP by providing data for action. There is a knowledge gap in Sweden that needs to be addressed in regard to understanding driving factors and barriers influencing parental vaccine acceptance as well as determinants of non-timely vaccination. Practical and effective tools to tailor programs and interventions for increased uptake might be needed to address potential barriers to vaccinations. The experience of the TIP project initiated by the PHAS will be valuable for providing evidence of the application of the tool in a Swedish context. Scientific evidence on the impact of strategies to address vaccine acceptance and suboptimal vaccination coverage is essential. For the management and implementation of the NIP, methods to systematically inform about vaccine acceptance need to be implemented to sustain high vaccine acceptance, coverage and resilience in the future and to have effective tools to address low uptake in the Swedish context when needed.

Aims

This thesis aims to provide an in-depth understanding of current parental vaccine acceptance, focusing particularly on HPV and MMR vaccinations to further identify factors influencing low vaccine acceptance and to evaluate a tailored intervention to improve vaccine uptake. The purpose of the studies is to develop evidence-based methods to systematically inform the management and implementation of the National Immunization Program in Sweden regarding parental vaccine acceptance.

Specific objectives:

- To examine parental vaccine acceptance within the Swedish population regarding childhood vaccinations included in the NIP.
- To explore driving factors and barriers to parental vaccine acceptance.
- To assess socioeconomic and demographic factors associated with non-timely vaccination against HPV for parents of girls born 2002-2010.
- To describe and evaluate tailored interventions implemented for MMR vaccination targeting nurses at child health care centers in Rinkeby and Tensta (Stockholm, Sweden) working within a Somali community with low vaccine acceptance.

Research Approach

This section provides an overview of the study design and methods used for each respective study (Table 3). The study designs include both qualitative and quantitative methods.

Table 3. An overview of the studies included in this thesis.

Paper	Aim	Study Design	Data collection	Participants/target group	Analysis
I	To examine vaccine confidence and attitudes towards childhood vaccinations included in the NIP among parents in Sweden as well as to assess parents use of and trust in information sources regarding vaccinations.	Quantitative	Cross-sectional web-based survey	Parents to children aged 0-15 years	Descriptive, logistic regressions
II	To assess parental vaccine acceptance for vaccinations in the NIP and explore factors contributing to the high vaccine acceptance in Sweden.	Qualitative	Focus group discussions	Parents to children aged 1-2 years and 8-12 years	Content analysis
III	To examine HPV vaccination for girls in Sweden born 2002-2010 by assessing socioeconomic and demographic factors of the girl and parents associated with not being timely vaccinated in grades 5-6 and for receiving a delayed first dose of HPV vaccination by the end of compulsory school.	Quantitative	Registry-based, retrospective	Girls born 2002-2010 and their parents	Descriptive, Kaplan-Meier plots, logistic regressions
IV	To describe the formative research (Phases 1 & 2) and the intervention design and implementation (Phase 3 & Post-TIP) of the TIP project in Sweden targeting the Somali community.	Intervention design	Data compilation	Nurses working at CHCs in an area with low MMR uptake	Descriptive
V	To explore nurses' experiences of a tailored intervention that supported them with knowledge and tools to use during encounters and dialogue with parents with low vaccine acceptance.	Qualitative	In-depth interviews	Nurses employed at the child health centers involved in the intervention	Thematic analysis

Quantitative design (Study I & III)

Data sources

Hälsorapport – a web panel

Study I was conducted using a web panel run by the PHAS, “Hälsorapport” (Health report) (141). The panel was initiated in 2014 to provide a tool that facilitates surveys on public health topics relevant to the PHAS. Surveys have been sent to the participants on a monthly basis and periodically on a weekly basis for syndromic surveillance of influenza-like illness (ILI) and COVID-19. Participants in the web panel were recruited through a stratified randomized process of the Swedish population, which was stratified by age, sex, and geographic distribution. In 2016, a total of 10,000 guardians to children aged 3 months to 15 years of age were invited to voluntarily participate in the web panel on behalf of their child. In order to complete registration as a participant for the web portal, a set of background variables (including the age and sex of the child as well as parental educational level, country of birth and marital status) was provided.

National Vaccination Register (NVR)

The NVR was implemented on January 1st 2013 (142). The reporting of childhood vaccination included in the NIP to the registry is mandatory by law (2012:453), including HPV vaccinations for girls. The reports include a personal identification number (PIN) for each child, making it possible to link data with other sources. The PHAS is responsible for the registry. Data from NVR was retrieved up until May 31st 2023.

The Swedish Total Population Register (STPR)

The population register includes data on Swedish residents and is maintained and updated regularly by Statistics Sweden (SCB) (143, 144). The registry includes data on gender, date and place of birth, place of residency, date of death, family ties and dates for immigration and emigration.

Longitudinal integration database for health insurance and labor market studies (LISA by Swedish acronym)

The Longitudinal integration database for health insurance and labor market studies (LISA) includes all Swedish citizens aged 16 years or older (145). Data has been updated yearly since the 1990s. The database includes individual information such as income, education, and employment.

Study design and population

Study I

This cross-sectional study included all parents (1,046 parents) to children aged 0-15 years of age participating in the web panel “Hälsorapport” (Figure 11). All parents were sent a survey regarding attitudes towards vaccination. Attitudes to vaccinations were defined as “expressions of support or hesitancy” (43). The research team developed the survey to meet the specific aim of the study. Questions and items used in previous studies conducted in Sweden in 2009 and 2013 (29) and internationally were adapted for the study (35, 36, 39). A total of 12 items and 3 follow-up questions were included in the final version of the survey. The main topics of the items included: self-reported vaccination status of the child, reasons for hesitancy or concerns, perceptions of safety for vaccines and severity of childhood diseases, use of and trust in information channels as well as intention to vaccinate in the future.

Based on the responses in the survey, parents were classified into three groups:

- acceptors; vaccinated with all vaccinations offered within the NIP,
- questioning acceptors; vaccinated but responded feeling hesitant towards at least one vaccination,
- selective refusers: actively refused or delayed at least one vaccination for reasons other than medical reasons.

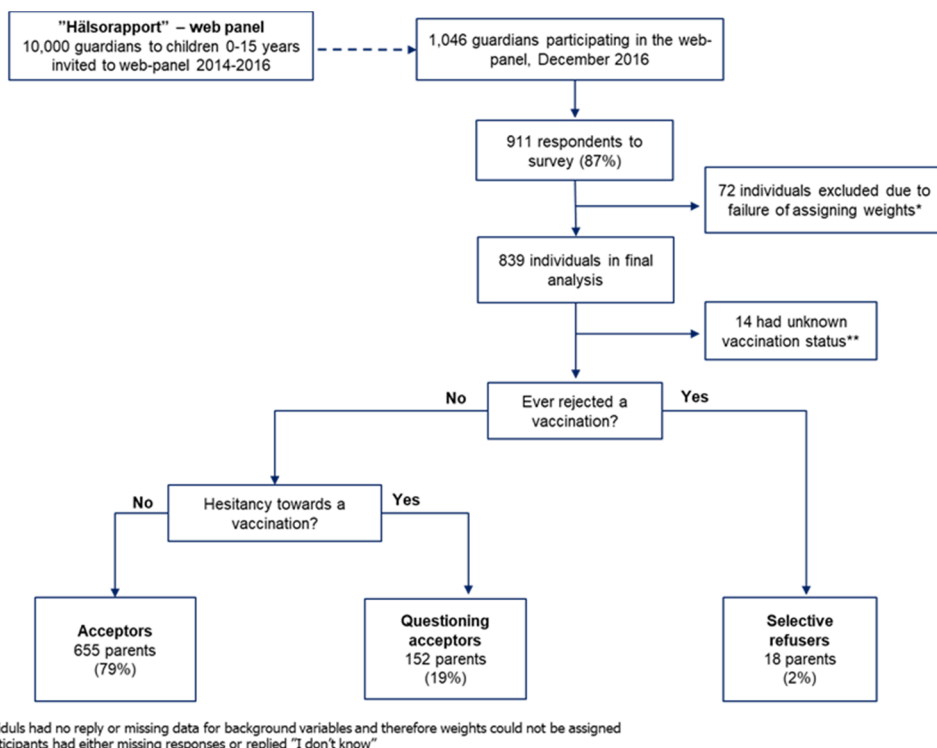


Figure 11. Flow chart of participants in study I.

*Individuals had no reply or missing data for background variables and therefore weights in the analysis could not be assigned

** Participants had either missing responses or replied "I don't know".

Study III

This registry-based retrospective study included all girls born from 2002 to 2010 and registered in the STPR. Girls residing in Sweden during the period corresponding to grades 5 and 6 in schools for which the HPV vaccine is offered were included in the study. The corresponding time to grades 5 to 6 was defined to start on August 1st of the year the girl turned 11 years old and ended on May 31st of the year she turned 13 years old. The dataset included data from STPR, LISA and NVR. Girls were excluded from the study based on dates of immigration, emigration and death.

Non-timely vaccination was defined to include girls not vaccinated for HPV in grades 5 and 6 according to the NIP schedule, as well as girls receiving a delayed HPV vaccination after grade 6 up until the end of compulsory school in grade 9. Hence, two different outcomes for non-timely vaccination were assessed. Based on HPV vaccination status (vaccinated or not), timely HPV vaccination was defined as having a record of vaccination for at least one dose of HPV vaccine at ages 11-13

years. The outcome of non-timely vaccination was thus defined as a lack of record of vaccination during the same period. As unvaccinated girls at the end of grade 6 can get vaccinated free of charge up until the age of 18, the outcome of delayed vaccination was assessed for girls born 2002-2007 up until the end of compulsory school in grade 9. Delayed vaccination was defined as receiving at least one dose of HPV vaccine within 3 years after May 31st of the year of the girl's 13th birthday.

Variables used for the analysis included birth year for the girl and country of birth for the girl and parents, as well as the parent's educational level and disposable income. The region of residency for the girl reflecting the time of eligibility for HPV vaccination according to NIP was also included in the analysis. A complete case criteria was applied and all categories with missing data for the variables in the final analysis were excluded except for the parental educational level. The inclusion and exclusion of girls in the study population for the final analysis are shown in Figure 12.

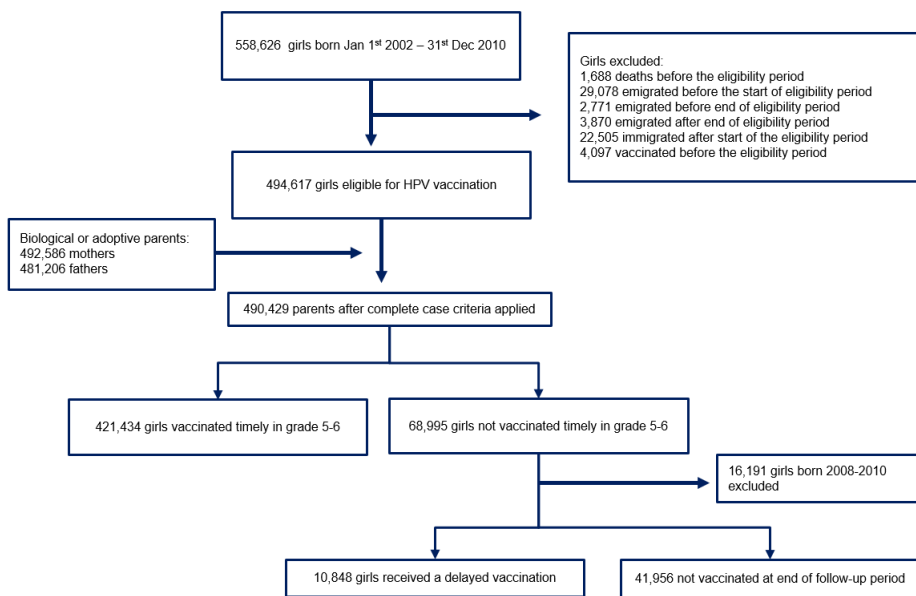


Figure 12. Selection of study population of girls eligible for HPV vaccination according to the NIP schedule in grades 5 and 6.

Methods for analysis

All statistical analyses were performed in Stata Statistical Software release 14 or 18 (146).

Descriptive statistics and Pearson χ^2

Descriptive statistics was the starting point for both studies to understand and get a sense of the data before moving on to further analysis. The Pearson χ^2 was used to make a comparison of descriptive statistics and assess differences.

Logistic regression

Logistic regression was used to assess the association of one dependent (outcome) binary variable and one or additional independent variables. Crude and adjusted multiple logistic regressions were used to calculate odds ratios (OR) and 95% confidence interval (CI). The logistic regression does not take the follow-up time into consideration.

Kaplan-Meier plots

Kaplan-Meier plots were used to describe the cumulative uptake for the first dose of HPV vaccination for each cohort of girls in **study III**. The differences in follow-up time were considered in the failure functions.

Qualitative design (Study II, IV & V)

The Tailoring Immunization Programmes approach

Study IV

The TIP project in Sweden described in this thesis was initiated in 2013 and focused on a Somali community in Rinkeby and Tensta in northern Stockholm. The area has lower MMR vaccination coverage, around 70% since 2002, compared to the national vaccination coverage above 95% (Figure 13) (147). In the districts, a high percentage of residents have foreign backgrounds, approximately 30% of whom are of Somali origin (147). There are two CHCs in each respective district. The TIP project has focused on the Somali community for the design and implementation of tailored strategies aiming for long-term behavioral change and increased MMR vaccine uptake.

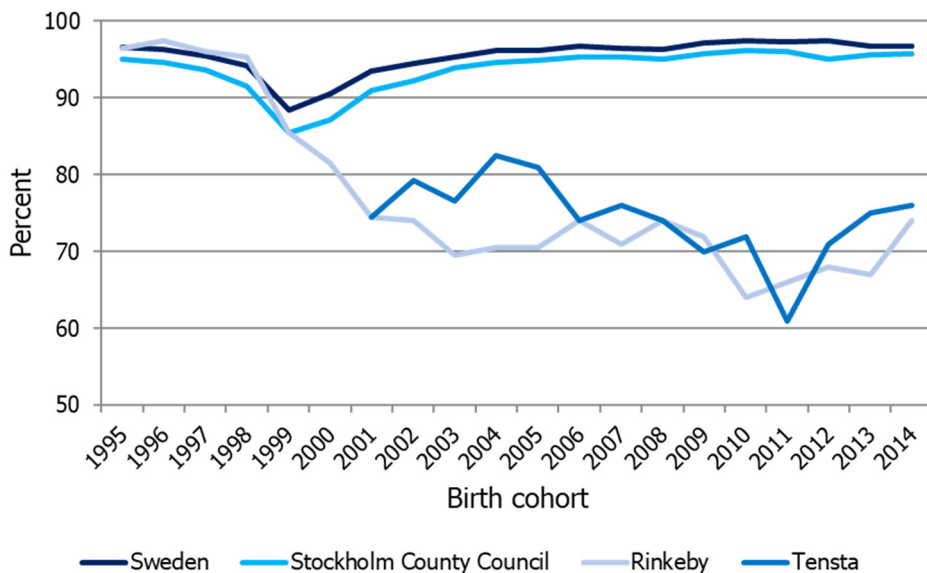


Figure 13. The national, regional and local vaccination coverage of the MMR vaccine in Sweden for children born in 1995-2015.
Source: Folkhälsomyndigheten

TIP phase 1 and 2 – situation analysis and research

The phases of the TIP project in Sweden are outlined in Figure 14. The situation analysis (phase 1) aimed to get an overview of the existing evidence regarding driving factors and barriers to MMR vaccination. This phase also included the support of stakeholders.

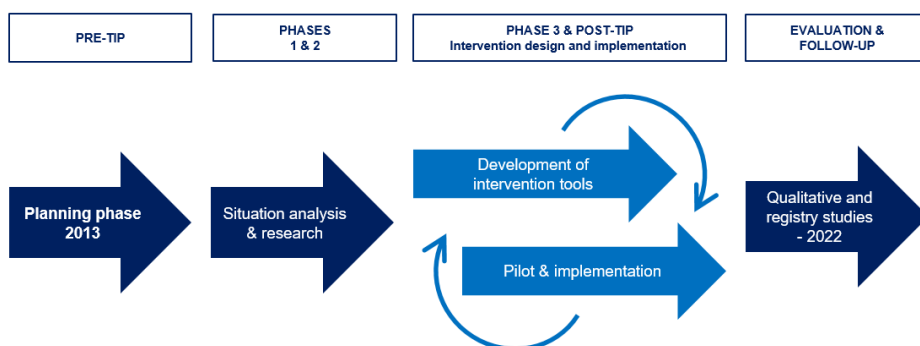


Figure 14. Overview of the phases included in the tailoring immunization programs (TIP) project in the Somali community in Sweden.
Source: An adapted version of the previously published figure in study IV (148).

For the next research phase (phase 2), qualitative in-depth interviews were conducted to gain further insight from the perspective of parents and nurses at the two CHCs in the community. The results for the Somali parents were mapped according to the COM-B model of the TIP approach to gain an overview of the barriers and drivers for vaccination behaviors among parents of Somali origin in Rinkeby and Tensta for the 1st dose of MMR offered in the NIP (Figure 15). Barriers to vaccination were seen across all three factors, while drivers were reflected in factors of motivation and opportunity.

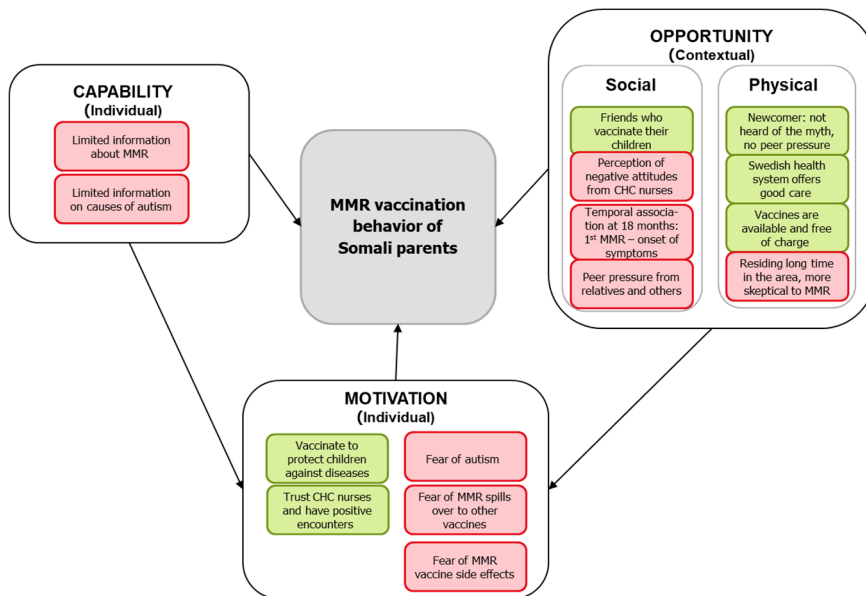


Figure 15. Conceptual map of driving factors and barriers to MMR vaccination. Driving factors are green and barriers are red.

Source: Jama et al, 2022 (148)

The results revealed that parents in the Somali community feared that children would “stop talking“ and develop autism and therefore delayed MMR vaccination (102). Despite the lack of scientific evidence (52, 53), the myth of MMR vaccination causing autism had been rooted for years and continued to circulate in the community. Although parents would attend appointments at CHC for baby checkups, they would refrain from attending the 18-month appointment at which the MMR vaccination is offered as part of the NIP. Hence, convenience and access to vaccination services were not deemed a main barrier to vaccination as parents attended the CHC services generally and received other vaccinations offered at the CHCs. The interviews with nurses highlighted that the nurses did not address parent concerns regarding MMR vaccination (103). This indicated a need for further

support for CHC nurses to improve communication and dialogue with parents with low vaccine acceptance.

Using the conceptual COM-B mapping, key barriers to MMR vaccination identified to address were knowledge among parents (capability), fears (motivation) and negative social pressure (social opportunity). For the CHC nurses, the key barriers to address were identified as a need for training as well as skills and confidence for engaging in vaccination conversations with parents having low vaccine acceptance (capability). Consequently, Somali parents of children aged 0-5 years and CHC nurses were identified as the two target groups for the intervention. In this thesis, the focus hereafter is only on the intervention activities targeting CHC nurses. The activities targeting Somali parents and the evaluation will be presented elsewhere in time.

To identify intervention functions, an adaptation of the Behavior Change Wheel (BCW) framework for vaccination behaviors was used (64, 149). The BCW framework includes three levels: sources of behavior, intervention functions and policy categories (Figure 16). The intervention functions link the barrier to vaccination and its COM-B factors with suggested interventions that can impact the vaccination behavior to be addressed. The third and final level suggests options at the policy level that could support the interventions.

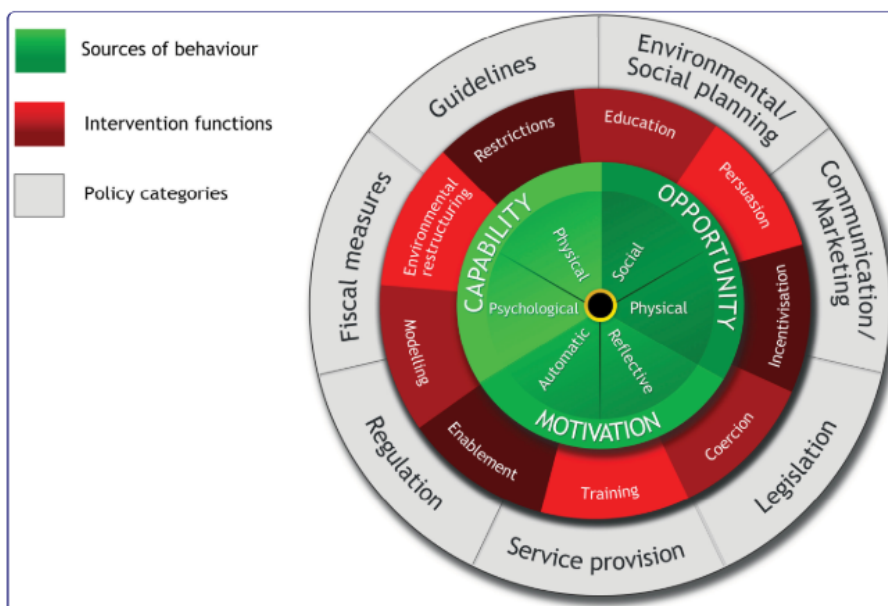


Figure 16. Overview of the behavior change wheel framework.
Source: Michie et al, 2011 (149)

Study design and population

Study II

Six FGDs were conducted with parents of children aged 1-2 and 8-12 years. The methodology of FGDs was chosen to understand vaccine acceptance for vaccinations from the perspective and experiences of parents, which is in line with the purpose of the study. In the FGDs, the interactions among the participants generate additional value for the discussions by exploring the topic further. The use of FGDs is especially favorable when assessing experiences, opinions and norms or complex behaviors (150).

Parents of children in the respective age group were invited to participate in three FGDs. Purposive sampling was used recruiting parents to include various views, perspectives, and experiences among the participants. Variance in terms of sex, educational level, income and country of birth was strived for. The FGDs were conducted in different geographical areas (southern, middle and northern parts of the country) to enrich the diversity of the participants. A phone registry was used to invite parents to the study. An inclusion criterion was the experience of vaccinations for their child; thus, they had to be part of the decision-making process for their children's vaccinations. To be eligible for the study, parents should have accepted at least one vaccination for their child and been part of the decision-making process.

Experiences of childhood vaccinations (including HPV for parents to older girls), VPDs, parental decision-making, information for informed decisions, and trust in information sources were included in the FGD guide. In total, 47 parents participated in the FGDs. All FGDs were audio recorded and the sessions ranged between 88 and 116 minutes, with an average of 108 minutes.

Study V

In-depth interviews were conducted to evaluate the intervention implemented for the nurses. A qualitative in-depth interview approach was chosen to explore and capture the nurses' experiences and understand their point of view of the implemented intervention. In-depth interviews are particularly useful for understanding the participants' points of view and experiences and hence, a suitable evaluation method (150).

All nurses working at the CHCs involved in the intervention were invited to participate in the in-depth interviews in November 2017. The purpose, design, and methodology of the study were shared with the nurses in advance. The interviews were semi-structured, following a thematic guide. The guide was informed by a previous study along with responses to a survey conducted at the wrap-up of the final seminar of the series (103). Topics in the guide included personal experiences of the interventions, their usefulness, and changes in their work since the intervention. The nurses' perception of the parents' experiences with the

interventions was also included. Two researchers piloted the interview guide, after which minor reorganizations of items and additions of probing questions were made to facilitate the flow of the interviews. Interviews were audio recorded and ranged from 18 to 43 minutes, with an average of 34 minutes. All interviewees were asked to choose a location for the interviews where they could feel free to talk openly.

Methods for analysis

Content analysis

Content analysis was used to analyze the FGDs in **study II** as the method allows for interpreting and understanding the data's manifest and latent meaning (151). All FGDs were transcribed verbatim. The recordings of the FGDs were listened to repeatedly, and transcripts were read several times so that the researchers could thoroughly understand the material before conducting the analysis. The FGDs, with the respective age groups of children, were analyzed separately as the vaccinations are implemented in different settings; CHCs versus school health services. Transcripts were coded initially and thereafter, similarities and differences of codes were considered for generating subcategories and categories. In the final stage of analysis, themes emerged to reveal the latent findings of the material. Subcategories, categories, and themes were discussed frequently amongst the research team in meetings and peer debriefings during the analysis. Subsequent revisions of the results were made following the discussions until the final results were agreed upon. Analyses were conducted in Microsoft Excel.

Thematic analysis

All in-depth interviews for **study V** were transcribed verbatim. As the implementation of intervention activities and tools was of particular interest to the aim of the study, thematic analysis was chosen to allow for emphasis on these analytic interests (152). Initial coding was generated by one researcher and thereafter, the codes were shared and discussed with another researcher to assess the consistency. The codes were then assessed and themes emerged. An example of the analytic process is provided below (Table 4). Drafts of themes were discussed among additional research team members to elaborate further and revisions were made until final themes were agreed upon. The analysis was conducted using Microsoft Office Excel as well as manually.

Table 4. An example of the analytic process.

Text	Code	Subtheme	Overarching theme
But then it probably has with a lot of things to do, maybe with me, that I'm secure in my professional role and also all the work that has been done in various ways.	Different things that make me secure in my professional role	Feeling more confident to address parents' MMR vaccine concerns	Perception of improved communication with parents

Ethical considerations

Ethical review boards have approved all studies included in this thesis. Studies were conducted in accordance with regulations stipulated by the Declaration of Helsinki. For each study, only a restricted number of researchers had access to the collected data. Data was stored securely to prevent unauthorized access to data. Results for all studies are presented at an aggregated level so that an individual's identity cannot be revealed and that personal integrity is ensured.

Study I

Stockholm Regional Ethics Review Board (No. 2016/1752-31/4) approved the study. Participation in both the web panel and the survey was voluntary. Voluntary participation in the survey was emphasized when parents were invited to the study. In addition, the survey included an opt-out alternative for all questions, e.g. "I do not want to answer", so that participants could choose not to respond to specific questions. Participants responded to the survey anonymously and no personal identifiers were included in the dataset, all respondents were given an observation number to use for analysis.

Study II

The Swedish Ethical Review Authority (Dnr 2019-00122) approved the study. All data collected was anonymized to ensure that individuals could not be identified. Before starting the FGDs and data collection, all participants had to provide written informed consent to participate. The informed consent included information about the study, their rights as participants and voluntary participation, and how results would be used. In order to promote an atmosphere that facilitates open discussion, only parents who had accepted at least one vaccination for their child were invited. Thus, the research team strived to generate stimulating discussions and prevent loaded, conflicting views.

Study III

The Stockholm Regional Ethics Review Board approved the study (Dnr 98-002: Dnr 02-556; Dnr 2012/216-32). When conducting the registry-based study, no informed consent is feasible or required from the participants. Rather, the use of registries for research is regulated by law (153). To protect the integrity and the individuals, SCB used the PINs to link individual data from each data source and then replaced the PIN with a random and unique numeric code before data was given to researchers. Members of the research team have no access to the key kept by SCB. Hence, the researchers with access to the data only had a de-identified dataset for the analysis to limit the possibility of identifying specific individuals and reinforce confidentiality.

Study IV & V

The Stockholm Regional Ethics Review Board approved the interview study with the nurses (Dnr 2016/1518-31/5). The studies conducted in the initial phases of the TIP project were approved previously (Dnr 2013/678-31/3). Written informed consent was obtained from all participants before the start of the interviews. To ensure the anonymity of the nurses, all potential personal identifiers were anonymized when transcribing the interviews. Each interview was given a unique number as identification, and only researchers conducting the interview could access the key. Each participant was asked to choose the location for their interview to support an atmosphere for open and private discussions. All nurses chose to conduct the interviews at their respective workplaces. Participants were informed both orally and written that participation was entirely voluntary and that they could end their participation whenever they wanted without any negative consequences.

Main results

General parental vaccine acceptance for the NIP

Societal perspective and norms

Parents wanted to *vaccinate to do good for the individual and society (theme, older children)* (Table 5), in **study II**. Solidarity motivated vaccination from a community perspective to protect the health of the individual and others, including the most vulnerable in society. Examples were also given for when other parents did not show solidarity by vaccinating their children, which triggered a dichotomous view of “we versus them”. Parents also perceived that the group of unvaccinated children in Sweden was increasing.

“won’t be a carrier of disease and put others who are weak at risk...even though my child has a good immune system and can get through the struggle of going through a disease”

”as more and more choose not to vaccinate... and as [my child becomes] adults they can become sick anyways as their own protection from vaccination decline”

Parents also expressed *strong compliance to and protection of the value of vaccinations* (theme, younger children) (Table 6). This was reflected by both the trust in the system for the NIP and the services implementing the program. Feelings of gratitude were expressed for being offered health-promoting vaccinations for their child free of charge. A societal norm for vaccinations was also highlighted as parents followed the recommendations and accepted vaccinations automatically (passive decision).

”I also trust there is a reason for implementing a large national program”

“just like a child car seat, it is [vaccinations] the safest option in most cases”

A solid foundation is built with nurses at CHCs

Results in **study II** showed that *a foundation of trust is built at CHC for decisions later on* (theme, older children). Parents described that *an attentive relationship with their CHC nurse made them feel safe* (theme, younger children). Although there was diversity in the encounters and experiences differed, positive encounters built safe and trusting relationships. A responsive and understanding dialogue was needed for parents to feel attuned and listened to regarding their individual perspectives and context. Parents also valued the practical skills of the nurses, including using pain relief strategies for the child when being vaccinated as the vaccination situation might be emotionally charged for the parents and painful for the child. As the vaccination services shifted from CHC to school, the parents perceived the decision to vaccinate shift from mandatory in CHCs by oral consent to be more active and voluntary as written consent needed to be signed.

”when the children were younger, it was easier to make decisions and I felt safe making them and could relate to it in a positive way”

”much depends on the CHC-nurse, if the nurse is good you get good information and if she is not knowledgeable you don’t get any information”

Changes as the child gets older

As the child got older, parents perceived *the decisions for vaccination become more complex* (theme, older children). More questions were expressed regarding the school-age vaccines, including HPV, compared to the early childhood vaccines. Daughters also played a central role in the decision for HPV vaccination, putting parents in a new situation for involving them in the decision-making process and addressing their questions and concerns. The fear of and temporary pain of needles and emotional aspects of the vaccination itself were also seen as challenges by parents to school-aged children.

“I believe it was more difficult to make decisions regarding the vaccinations offered in school”

”as children become older and part [of the decision] too, they have questions and concerns themselves...more questions makes it [the decision] more difficult”

The spectrum of parental vaccine acceptance

In **study I**, the spectrum of vaccine acceptance is reflected by the categorization of parents according to the self-reported vaccination status of their child and having questions and concerns regarding vaccinations for their child. The majority of

parents, acceptors (79%), vaccinated without any doubts, followed by questioning acceptors (19%) who felt hesitant or had concerns for at least one vaccination but still had vaccinated their child (Figure 17). A low proportion of parents were selective refusers (2%) who had actively refused at least one vaccination for their child. None of the parents had refused all vaccinations offered in the NIP. Slight differences were seen between acceptors and questioning acceptors, whereas more negative perceptions regarding vaccinations were observed for selective refusers.

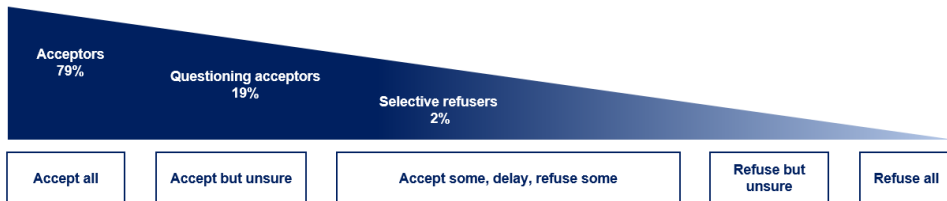


Figure 17. The results of study I along the spectrum of vaccine acceptance.

Vaccinations for health and protection against VPDs

In **study I**, 97% of the parents agreed that it is important to vaccinate for the health of the child and 95% for the health of other children. In addition, parents also agreed that vaccinations are protective against diseases (97%) while disagreeing that vaccination itself poses a greater threat to health than VPDs (94%). In **study II**, parents perceived that vaccinations protect against diseases, some being potentially life-threatening diseases, including cancer. Detailed knowledge, however, about diseases was lacking. Parents also felt a sense of safety and comfort knowing their child would be protected against diseases.

Questions and concerns about vaccinations

In both **studies I and II**, parents had questions and concerns about vaccinations. In **study I**, adverse events were the main reason for hesitancy or refusing a vaccine. Of all parents, 21%, either had concerns or refused a vaccination in the NIP. Worrying about adverse events, having read or heard negative information, and lacking good and reliable information about vaccinations were the main reasons for questioning or refusing a vaccine. The same top three reasons were also seen when responses for the HPV vaccine were excluded. Concerns were primarily related to HPV (35%) and MMR vaccination (26%) for parents being questioning acceptors. Questioning acceptors vaccinated despite feeling hesitant due to the trust in nurses at CHCs and in the recommendations given. Other reasons given for vaccination were feeling group pressure or wanting to avoid the diseases. The vaccinations that were refused were mainly HPV (70.8%), followed by vaccination against

pneumococcal disease (24%), and MMR (23%). The aspect of convenience was only given as a reason for not vaccinating by one parent.

In **study II**, different reasons for having questions and concerns were given. More specific examples were perceiving vaccines as new, the content of the vaccines, financial and commercial incentives and rumours of potential adverse events. Concerns were also more general, such as worries about making the wrong decision or worries and feeling that “what if” unexpected adverse events in the future, especially relating to the HPV vaccinations. Overall, the positive aspects of vaccination outweighed parents' questions and concerns about vaccinating their children.

”A vaccine can be good at the moment and one can read about it [about vaccine safety], but once you take the vaccination, what will happen in a few years time?”

Information sources and requested information by parents

Nurses at CHCs were the most used source of information for all parents in **study I**. The official Swedish healthcare information hub “1177” was also frequently used by all as well as the school health services. Differences were seen between the groups as the proportion searching for information online was mostly used by selective refusers, followed by questioning acceptors and, to a lesser extent, by acceptors. Trust in sources of information differed among the parental groups. Acceptors trusted mostly health professionals and pamphlets at CHCs and schools, the PHAS, and the “1177”. Only slight differences were seen for the questioning acceptors. The trust in nurses at CHCs differed notably between the groups. In contrast, information searches online were most trusted by selective refusers, followed by the “1177” and physicians at CHCs. Nurses at CHCs and social media were the least trusted sources for selective refusers.

The results of **study II** revealed *a spectrum of communication needs for parents that is essential to be met* (theme, younger children), while the *communication also changes as children get older and needs to be explicit and tailored* (theme, older children). The spectrum ranged from parents not wanting much information at all to those requesting in-depth information and scientific details. Hence, the content, amount, and timing of information, formats (digitally, paper-based, or orally), and sources of information requested were diverse and differed among parents. Requests were made for information to be explicit and tailored. Although searching online was common, parents experienced difficulties in assessing the trustworthiness of the information. The “1177.se” website was highlighted as frequently used as a trusted source of information. Other examples of information channels were family and friends, as well as communicating online with other parents.

”I try to only use 1177, otherwise there is too much [information] out there and you need a PhD to assess what’s true or not ”

In **study I**, responses to an open-ended question (49% responded) primarily showed that parents requested transparent, unbiased, and trusted sources of information without the influence of pharmaceutical companies. Parents in **study II** also requested transparent information and scientific evidence presented objectively, including positive and negative information regarding vaccinations and acknowledging possible adverse events and knowledge gaps.

“transparent information, including what is not known,.. communicated in a good, broad way [for all]...so that I can choose myself “

Study II also highlighted a shift in the information provided about vaccinations in schools. Instead of parents receiving information directly from the vaccinating nurse at CHCs, parents received written information in schools. Children were a main information channel between the school and the parents and a primary transmitter of information, especially for HPV vaccination. Parents of school-aged children wished to receive information themselves first-hand. Oral information and the possibility of meeting the school health nurse and other parents to discuss vaccinations were asked for.

”just got informed that it [vaccination] would take place...the school was just the transmitter of information and what would happen regarding vaccination in grade 5”

Table 5. Overall results results of themes and categories from from focus group discussions with parents of children aged 8-12 years.

Theme	Category
Vaccinate to do good for the individual and society	Contribution to the community to protect the health of the individual and others Protect against serious diseases “We against them” mentality
A foundation of trust is built at CHC for decisions later on	Safety and trust in NIP and CHC
Decisions for vaccination become more complex as children get older	Vaccinations concerns shift as the child gets older and play a central role in the decision for HPV vaccination Challenges with vaccinations and worries for the future, although expressing positive aspects for vaccinations overall
Communication changes as children get older and need to be explicit and tailored to the situation	Need for transparent information for everyone Parents prefer and relate differently to information sources The child is a primary transmitter of information, especially for HPV vaccination

Table 6. Overall results of themes and categories from focus group discussions with parents of children aged 1-2 years.

Theme	Category
Strong compliance to and protection of the value of vaccinations	Trust in the national immunization program Feelings of safety and solidarity motivate vaccination
Parents feel safe with an attentive relationship with their nurse	Diversity in how nurses encounter parents Need for responsive and understanding dialogue Practical vaccination skills are valued by parents
The spectrum of communication needs is essential to meet	Different needs of content, amount, and timing of information to feel prepared for a vaccination offer Diverse information channels and formats are needed Risk perception and sense of disease severity for vaccine preventable diseases

HPV vaccine uptake in focus – determinants for non-timely vaccination

Results in **study III** show that of girls born 2002-2010 (n=490,429) 86% had received their first dose of HPV vaccination in grades 5 to 6 according to the NIP and 14% were not vaccinated during the period. The vaccination uptake (1st dose) at the end of 6th grade increased from 82% for girls born in 2002 to 92% for girls born in 2010 (Figure 18).

Factors associated with non-timely vaccination in grades 5 and 6

The birth year of the girl, the country of birth for the girl and parent, as well as the disposable family income and educational level of the parents, were associated with non-timely vaccination in grades 5 and 6 based on the multivariable analysis. Compared to parents having a high income, a disposable family income in the lowest tertile, (OR 1.68 [95%CI: 1.64-1.73]) or medium tertile (OR 1.41 [95%CI: 1.39-1.44]) was associated with non-timely vaccination. Compared to parents having a post-secondary education, not being vaccinated was associated with a high school education (OR 1.16 [95%CI: 1.14-1.18]) as well as parents not having an education in the registry (missing category) (OR 1.37 [95%CI: 1.24-1.50]). The birth year had a stepwise downward trend associated with non-timely vaccination (Figure 19). Girls born in 2003 and 2004 had the strongest associations for not being vaccinated while the birth years of 2006-2008 were all associated with timely vaccination, for which the association increased for each birth year.

Compared to girls and parents born in Sweden, all other combinations of country of birth examined were associated with non-timely vaccination by the end of grade 6 (Figure 20). Regardless of the girl being born in Sweden (OR 1.40 [95%CI: 1.37-1.44]) or abroad (OR 1.59 [95%CI: 1.46-1.72]), having one parent born abroad and

one in Sweden was most strongly associated with not being vaccinated by the end of grade 6. Additionally, girls born in Sweden with parents born abroad (OR 1.55 [95%CI: 1.51-1.59]) were also associated with not being vaccinated.

A sub-analysis of girls born in 2010 also showed pronounced differences despite being the most recent cohort being offered HPV vaccination while a gender-neutral program had been implemented.

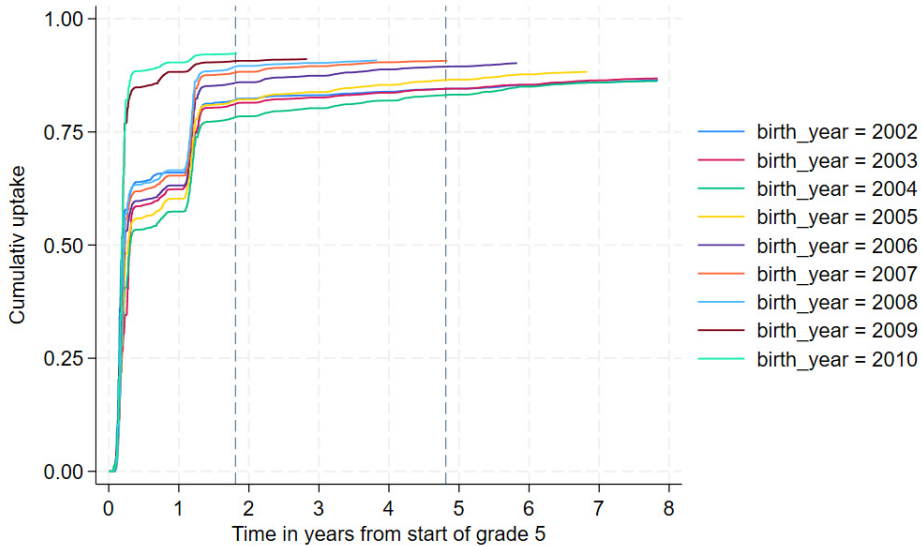


Figure 18. Kaplan-Meier plot of the cumulative uptake of the first dose of HPV vaccine during 5 years, from the start of 5th grade up until the end of grade 9 in compulsory school. The end of 6th grade is indicated by the dashed line.

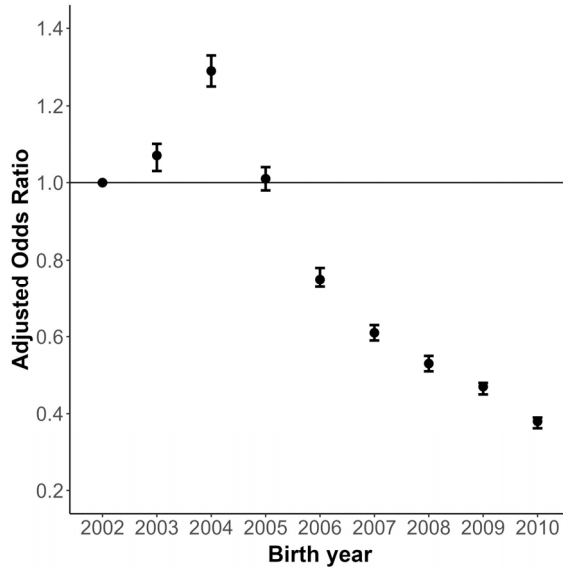


Figure 19. Multivariable analysis of birth years for girls born 2002-2010 for odds of not being timely vaccinated according to the NIP in grades 5 and 6.

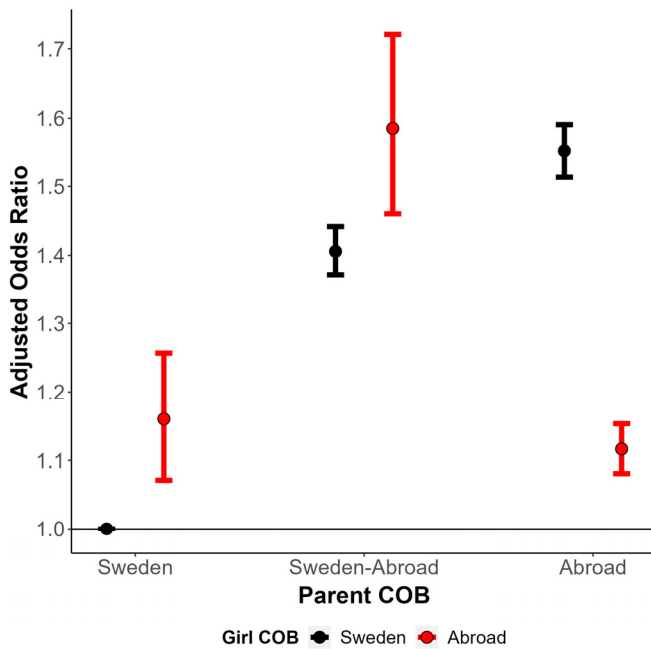


Figure 20. Multivariable analysis by country of birth (COB) of the girl and parents combined for the outcome of non-timely vaccination in grades 5 and 6.

Factors associated with delayed vaccination up until the end of compulsory school (9th grade)

Of the girls not receiving a vaccination in grades 5 and 6, additional analyses were conducted to assess factors associated with delayed vaccination after grade 6 up until the end of compulsory school in grade 9. The cumulative uptake for receiving a delayed vaccination is shown in Figure 21. In total, 18% of the girls had been vaccinated within three years or less. As girls born in 2008 and 2009 had not graduated 9th grade, they were not included in the final analysis for delayed vaccination. When taking the delayed vaccinations into consideration, the overall vaccine uptake of the first dose of HPV vaccination reached 88% for girls born between 2002-2010.

Multivariable analyses were conducted to further assess factors associated with receiving a delayed vaccination for girls born 2002-2007 (n=52,804). Receiving a delayed vaccination was associated with the birth year of the girl, parental educational level and country of birth. All birth years for the girls showed an association in comparison to girls born in 2002, for which birth years 2005 and 2006 had the strongest association. Girls having parents with 9 years of schooling or less (OR 1.44 [95%CI: 1.31-1.57]) were most strongly associated with receiving a delayed vaccination in comparison to parents having a high educational level. Girls born abroad who also had their parents born abroad (OR 1.64 [95%CI: 1.52-2.78]) as well as girls being born abroad and their parents born in Sweden (OR 1.48 [95%CI: 1.24-2.77]) were the most associated with getting a delayed vaccination in comparison to girls and parents born in Sweden.

Girls not being vaccinated neither in grades 5 to 6 nor by the end of compulsory school in grade 9, was associated with parents having a high school education (OR 0.72 [95%CI: 0.68-0.75]) or low (OR 0.73 [95%CI: 0.69-0.78]) or medium income (OR 0.75 [95%CI: 0.71-0.79]). Girls being born in Sweden and having at least one parent born abroad (one parent abroad; OR 0.85 [95%CI: 0.80-0.91]; both parents born abroad OR 0.65 [95%CI: 0.60-0.70]) were associated with not being vaccinated up until the end of compulsory school in grade 9.

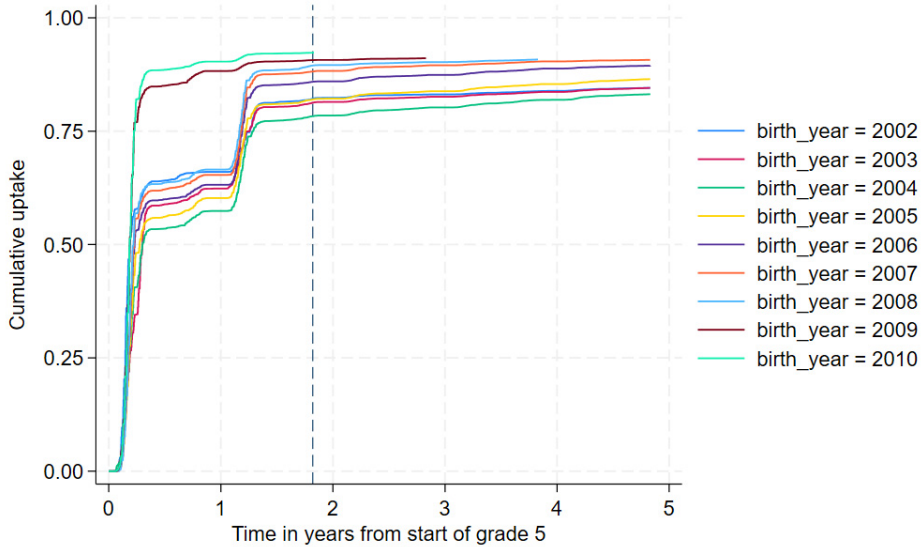


Figure 21. Kaplan-Meier plot of the cumulative uptake of receiving a delayed first dose of HPV vaccination after the end of 6th grade until the end of grade 9 in compulsory school.

The TIP approach – from design to evaluation of a tailored intervention

Based on the results of the situational analysis (phase 1) and research (phase 2), the subsequent TIP phase (phase 3) was initiated for the design of theory- and evidence-informed interventions in **study IV**.

The intervention was designed based on discussions of the activities for each of the intervention types identified by using the BCW model of the TIP approach. Subsequently, the key barriers and their associated COM factors were mapped to evidence-based interventions for addressing the barriers (Table 7). Selected intervention types targeting the CHC nurses were education and training. Education as an intervention type was defined as increasing knowledge or understanding, while training was defined as imparting skills (64). Ideas for activities were discussed based on the intervention types. Acceptability for the target group and the feasibility of budget and timeframe were also considered.

Table 7. Overview of the key barriers with the respective capability, opportunity and motivation (COM) factors, intervention types and selected activities for nurses in the intervention project.

Key barrier	COM factor	Selected intervention type	Selected activities
Need of training, skills and confidence for CHC nurses for difficult vaccination conversations	Capability	Education (nurses)	Information-based seminars with training
Perception of negative attitudes from some CHC nurses		Training (nurses)	Information-based seminars with training

Based on the identified intervention types and the suggested type of activities, a seminar series was deemed most appropriate to specifically target the nurses. The seminar series included strengthening the education of nurses regarding MMR vaccination and training on communication skills for their dialogue with parents. In addition, the seminars provided an opportunity for the nurses to meet, discuss and share experiences regarding how they work and interact with parents in relation to the MMR vaccination. A narrative film and intervention card were developed based on the intervention types primarily targeting the parents. The film and information card, however, were seen as tools that the nurses could use in their encounters with parents who had low vaccine acceptance, thereby facilitating the dissemination of the material to the parents. Therefore, the narrative film and information card were included in the intervention package for the nurses. Consequently, the intervention activities targeting nurses consisted of a seminar series, a narrative film and an information card. All 12 nurses employed at the Rinkeby or Tensta CHC were invited to participate in the activities at the time of implementation.

Seminar series - A series of three seminars were arranged during consecutive weeks in August and September 2015. Each seminar lasted 2 hours and covered different topics relating to MMR vaccination i.e., measles, MMR vaccination, communication, and autism.

A narrative film - "Vaccination – a wise choice for your child", a 14-minute film in Somali with Swedish subtitles (154). A physician, nurse, religious leader and parents shared their personal stories, views and experiences to promote vaccination as role models. The film included information about measles and MMR vaccination. When the film was published on YouTube in 2016, the nurses were provided with a link for easy access (154).

Information card - A two-sided information card was provided to nurses to use in their encounters with parents and distribute to them. The card consisted of key messages provided in Somali and Swedish on each respective side of the card (154). A link and QR code to the narrative film and a website with further information was included on the card.

Results from the process evaluation of the tailored intervention in **study V** revealed an overarching theme that nurses *perceived improved communication with parents* after the intervention. Nurses perceived a change following the intervention as they expressed *feeling more confident to address parents' MMR vaccine concerns* (theme). They felt more confident about engaging in dialogue and discussions with parents and replacing insecurity and hesitation about the MMR vaccine potentially causing autism with confidence in scientific evidence for the lack of causality. As nurses found new ways to discuss the MMR vaccine and could confidently communicate the strong scientific evidence that the vaccine does not cause autism, the dialogue with parents was facilitated. A challenge for the nurses was to balance between being proactive in the discussions with parents without feeling persuasive for parental decision-making.

“the more knowledge I have, the more confident I am to engage in discussions”
[nurse, #1]

“what if I vaccinate and they get autism?” I was feeling guilty... now I know, it doesn't cause autism” [nurse, #9]

The diverse tools developed for the intervention (seminars, film and information card) were perceived as *useful support to dispel myth and reduce language barriers* (theme). The seminar series was beneficial and valuable, according to the nurses. After the seminar series, the nurses felt more knowledgeable and equipped with practical tools for structuring discussions with the parents and approaching the discussions in new ways.

“had the greatest benefit of being able to separate and explain what autism is and what the vaccine is, in my dialogues with parents” [nurse, #6]

“I have found good arguments based on research and [I] can confidently tell it to others, indeed” [nurse, #10]

Nurses described the information card as useful when handed out directly to the parents. Using the card also ensured the nurses that parents received essential and correct information as the card had the same information provided in both Swedish and Somali. The film was perceived positively and used in different ways by the nurses. The film was seen as credible, with evidence-based information provided by experts and parents of Somali origin who speak Somali. The nurses perceived the film to decrease language barriers and facilitate a better understanding of the content. Nurses gave examples of occasions when parents either had changed their minds about MMR vaccination or felt that parents became less skeptical after watching the film. Following the intervention, the parents were more open to discussions and less questioning, according to the nurses' point of view. During the

measles outbreak in the spring of 2017, the card and film had been particularly handy and useful.

Discussion

Summary of key findings

The findings of this thesis contribute to an in-depth understanding of current parental vaccine acceptance for vaccinations in the NIP in Sweden, with a particular focus on HPV and MMR vaccinations. Factors influencing parental vaccine acceptance are complex and contextual. By using mixed methods, the quantitative and qualitative studies describe different aspects of parental vaccine acceptance 2016-2023. **Studies I and II** identified driving factors and barriers to parental vaccine acceptance. Most parents (79%) vaccinated their children without any doubts, while others (19%) vaccinated their children but had questions or concerns or declined at least one vaccination for their child (2%). Both individual and societal perspectives were shown to be driving factors in parental vaccine acceptance. Societal norms were also shown to influence parents to vaccinate as they had strong compliance with and were protective of the value of vaccinations. Parents did not only vaccinate their children for individual protection but also for solidarity and society. The confidence in vaccinations was high as parents perceived the vaccinations as safe and effective and trusted the system and nurses implementing the vaccinations. Additional findings highlight the nurses as the backbone of the NIP and how they interact and communicate with parents. Not only was trust built early on at CHCs but it was also a foundation for parents to rely on for vaccine decisions for school-age children. Nurses were also highly trusted and a primary source of information on vaccinations for parents. Barriers to vaccination were mainly related to safety concerns of adverse events or perceptions of negative or inadequate information. Concerns were particularly raised concerning the HPV vaccination, both in terms of safety and the fact that decisions were perceived to be more challenging as the child got older. Parents' spectrum of communication needs was highlighted as a challenge to meet.

Study III highlights the association of social determinants for HPV non-timely vaccination in grades 5 and 6, according to the NIP. In total, during the study period, 86% of the girls were vaccinated with one dose of the HPV vaccine, and 14 % of the girls remained unvaccinated at the end of grade 6. The coverage of the first dose of HPV vaccination increased from 82% for girls born in 2002, at the end of grade 6, to 92% for girls born in 2010. Not being vaccinated by the end of grade 6 was associated with parents having a low or medium disposable family income and only

a high school education as their highest education. Girls born in 2004 had the strongest association for not being vaccinated and the association subsequently dropped by birth year as girls born in 2010 had the strongest association to be vaccinated. Interestingly, all combinations of the country of birth were associated with not being vaccinated compared to girls and parents all born in Sweden. Girls who had one parent born in Sweden and one parent born abroad had the strongest association with not being vaccinated, regardless of whether the girl was born in Sweden or abroad. Girls born in Sweden with parents born abroad were also likely to not be vaccinated for HPV by the end of grade 6. A sub-analysis of girls born in 2010 also showed that the differences in social determinants remained also in the most recent cohort being offered HPV vaccination and following the implementation of a gender-neutral program. Factors associated with receiving a delayed vaccination before the end of compulsory school in grade 9 were also assessed. Getting a delayed vaccination by the end of compulsory school was associated with parents having 9 years of schooling or less. Girls born abroad who also had their parents born abroad as well as girls born abroad with parents born in Sweden was the most likely to get a delayed HPV vaccination.

The TIP approach was piloted to gain experience of a tool to tailor interventions for increased uptake of MMR vaccination in a Somali community outside Stockholm. Based on a theoretical framework, as described in **study IV**, the design of tailored interventions for nurses resulted in the development of a series of seminars, a narrative film, and an information card. The tailored tools were implemented from 2015 to 2017. After the intervention, **study V** showed that nurses felt more knowledgeable and confident addressing parental concerns regarding the MMR vaccine. The intervention tools were perceived as helpful in dispelling myths and reducing language barriers in dialogue with parents.

Parental vaccine acceptance

The results of **study I** showed that the majority of parents (79%) vaccinated their children without any doubts, whereas other parents had questions and concerns (19%) or refused at least one vaccine (2%). The three groups reflect different positions along the spectrum of vaccine acceptance. As stated in the definition of vaccine hesitancy, the position on the spectrum is specific to the context and related to time. It is important to keep in mind that the results from the cross-sectional study only reflect the specific time of the study. Parental vaccine acceptance is diverse and changing, and the acceptance can move along the spectrum in either direction in the next instant or shift from one vaccination to another. The survey in **study I** was reused for another study conducted in 2022 with a different web panel (110). The results were similar, as 16% overall responded that they had questions or concerns about vaccinations.

Interestingly, it was noted in a study in 2009 that 17% of parents in Sweden have doubts about vaccinating their children (29). A previous study has described a range of positions along the spectrum of acceptance for childhood vaccinations, which were described as unquestioning acceptors (30-40%), cautious acceptors (25-30%), or hesitant (20-30%) (155). In the results from **studies I and II**, parents convey a trust in the safety and effectiveness of vaccines and the NIP system itself, including the CHC and school health services, and hence, the confidence for childhood vaccinations in the NIP is high and the strikingly high coverage is the outcome. Other studies in Sweden have also identified parental trust in the NIP, the system and authorities (31, 156).

The social aspects and norms were also highlighted as drivers for vaccinations. The social norm of vaccinating as the “normal thing to do” is an important aspect also previously identified (10, 33), which was also seen in **study II** as vaccinating was just something parents did by just going along with the system without thinking twice about it, which should not be underestimated. In addition, emphasis on the value of vaccination for the individual and society was also a striking driving factor for vaccination as vaccinating for solidarity to protect others in society, in addition to acquiring individual protection for the VPDs, was revealed. Regarding the demand aspect, the situation in Sweden seems to relate most closely to passive demand. The vaccines were accepted, but there was not a vital element of advocacy by the parents to make vaccinations their right and responsibility. Interestingly, the parents in **study II** showed a “we against them”-mentality as they expressed a critical view of non-vaccinating parents. The heated feelings show how the vaccinating parents wanted to advocate and defend the value of vaccination in discussions about childhood vaccinations. Their perception of the group of children not vaccinated is worrisome as it is based on misconceptions, nearly all parents in Sweden still vaccinate their children. Very few of the results of **studies I and II** were related to structural aspects of the system for vaccination and thus, the practical barriers to vaccination are likely limited. Nonetheless, it is crucial that the NIP system continue to be perceived as convenient and easy for parents to utilize so that structural and practical aspects do not become a barrier in the future.

Challenges and barriers to vaccine acceptance

In terms of the main barriers to parental vaccine acceptance, worries about adverse events was the primary reason for concern or refusal of vaccination, according to the results in **study I**. Additionally, parents raised safety concerns and worries about adverse events in the future, particularly in relation to the HPV vaccination, in **study II**. Worries about unknown adverse events were also raised by parents shortly after the introduction of the HPV vaccine in the NIP (31). Concerns and worries about safety aspects have been the most reported reason for hesitancy in several review studies for Europe and high-income countries (33, 44).

Other Swedish studies regarding HPV for girls also highlights the complexity of HPV vaccinations (30, 32, 156). **Study II** suggested that parents' perception of vaccine-related decisions shifted as their children got older. Naturally, as the children age and mature, they also increasingly become stakeholders in decision-making. Parents described how they included their daughters in the process and discussions or had to find answers to their questions. In some cases, the girls also had expressed a strong point of view on whether or not to get vaccinated. Previous studies have also seen that parents have not included their daughters in the decision-making for the HPV vaccination (156). Similarly, parents of adolescent girls in France have been revealed to make the decisions about HPV vaccination and their daughters have had a passive role concerning the decision (157). The issue of parental consent needed for HPV vaccination in Sweden and the dilemma of the autonomy of the child has been discussed previously (158). According to the UN Convention on the Rights of the Child, which is also part of Swedish legislation, children should have a say, and their wishes should be considered in decision-making. Children have a right to information and participation in decisions regarding their health. As the children become adolescents and mature, they should be included with age-appropriate information and parents might need to be guided and supported on how to include their children in the decision-making process and discuss decisions as parental consent is currently needed for HPV vaccination in schools. A vital aspect is the possibility of getting a delayed vaccination for children not vaccinated according to the NIP schedule. The results of **study III** reveal that nearly one-fifth of non-vaccinated girls at the end of grade 6 got vaccinated with their first dose of HPV within the following three years, highlighting the importance of providing opportunities for NIP vaccinations throughout school. Particularly, as the girls mature and reach 18 years of age, they will eventually have the possibility to decide about their vaccinations before they graduate from high school, regardless of parental consent. The Patient Act in Sweden (Patientlag (2014:821)) also states that children's wishes should be increasingly considered in relation to their age and maturity.

The challenge of trustworthy and adequate information

The results of **study I** and the themes in **study II** highlights the challenges of providing adequate, trustworthy information to meet the broad spectrum of needs. Reading or hearing negative information about vaccinations and lacking good and reliable information were among the top three reasons for questioning or refusing vaccination in **study I**. Vaccination information provided to parents has been shown to influence their decision-making. Dissatisfactory, inadequate or insufficient information is a barrier to making informed decisions, as parents are left with questions or concerns (33, 47, 159, 160). Parents have been shown to be more likely

to postpone or decline vaccination for their children due to insufficient information (30, 161). The need for trustworthiness, transparency and a balance of positives and negatives in messages regarding vaccination has also been highlighted (33, 47, 159, 160). Parents in **studies I** and **II** asked for different amounts, content, type, and timing of information, which poses a challenge for the nurses and the NIP system in providing information that suits every need and request. Each individual nurse cannot be expected to have all the knowledge themselves to provide all elements of information, specific details or the type of information requested, but by being attuned to the needs of the parents, the nurse can guide parents to the information they are asking for from a plethora of information provided elsewhere. In the school-based system, the possibility of parents having a direct dialogue with the vaccinating nurses seemed limited. Parents have also raised a need for dialogue with the school nurses in previous studies on HPV (31). In the current landscape of information and digital communication with social media, the amount of information available also provides a challenge for parents, requiring them to navigate and assess the trustworthiness of the information. The information nurses provide can be valuable in helping parents assess information from other sources. It is essential to meet information needs so parents can make informed decisions regarding vaccinations for their children. Ideally, parents should feel they have trustworthy and satisfactory information that answers and meets their questions and concerns before making informed decisions regarding vaccinations. As the information field changes with time, new ways of providing information will become available and requested.

Nurses – the backbone of the NIP

Findings from **studies I, II, IV** and **V** highlights the key role of vaccinating nurses for parental vaccine acceptance and the NIP. Numerous studies conducted previously in other countries and contexts have also highlighted the critical role of nurses and health professionals in parental decision-making and vaccine acceptance (10, 33, 45, 161-166). Interestingly, parents even vaccinated their children despite feeling hesitant based on the trust of the nurses and the recommendation of vaccination, according to results in **study I**. Trust in recommendations is one of the main reasons for vaccine hesitant parents to vaccinate despite concerns (33). Trust and the ability to meet parents at their particular position along the spectrum of vaccine acceptance are crucial factors for parental decisions regarding vaccinations (33, 155, 159). The vaccine acceptance of the nurses and health professionals themselves have also been identified as a key factor as those who feel hesitant are less likely to recommend vaccinations and those who have a high vaccine acceptance or are vaccinated themselves or have vaccinated their children are also more likely recommend vaccinations for their patients (10, 33, 165, 167-170). This was partly reflected in **study V**, where nurses felt unsure to recommend the MMR

vaccine before the intervention was implemented. Therefore, they were also hesitant to engage in discussion with parents who had low vaccine acceptance for the MMR vaccine.

Nurses were identified as a primary and highly trusted source of information on vaccinations for parents in **studies I** and **II**, which is in line with previous studies (10, 29, 33, 49, 132). How nurses communicate and discuss vaccinations with parents is also a key skill that influences parental vaccine acceptance (162, 171). Nurses and health professionals engaging with parents in open and accepting discussions regarding vaccination and having a pro-vaccination approach have been highlighted to facilitate vaccinations (39, 162, 163, 171). How health professionals communicate with and encounter parents was also emphasized as a central aspect by parents in **study II**. The importance of a responsive and understanding dialogue by the nurses and for parents to feel seen and heard was emphasized in the findings. To support and increase vaccine acceptance, dialogue-based, multi-component, and tailored interventions have been suggested to be effective (172). This includes improved communication of healthcare workers, which has been suggested to be effective for increased vaccination coverage (173). As seen in **study V**, the evaluation of the tailored intervention and tools targeting nurses suggests that relatively simple tools can make a difference in how nurses engage in dialogues with parents who have questions and concerns regarding vaccinations or have low vaccine acceptance. Nurses even perceived a shift in parental views following the intervention. Consequently, supporting nurses in their dialogue with parents regarding vaccination is a central aspect of the success of the NIP. Continuous work is therefore needed to adapt to the need of the nurses. The nurses should have their confidence to discuss vaccination with parents reinforced and feel equipped with tools and information to use for the discussions with parents.

Inequity

As higher incidences of HPV-related cancer and low initiation of HPV vaccination in Scandinavia have been linked to the same social determinants, the group of girls at increased risk of cancer is not receiving protection against HPV. Further health inequalities might be seen later in life if the girls remain unvaccinated. All children should have the possibility to get vaccinated regardless of social circumstances and determinants. The results of **study III** show inequities relating to the first dose of HPV vaccination in the NIP despite the implementation of vaccinations in a school-based system, free of charge. The school-based vaccination system has previously been shown to be the by far most equitable mode of delivery for HPV vaccinations in Sweden so far (128). The result showed that differences in terms of social determinants and inequities also persisted for girls born in 2010, the most recent cohort being offered vaccination. Further assessment of barriers to vaccinations and

the reasons for not vaccinating is needed, identifying determinants is just an initial step toward understanding inequities. The identified characteristics of girls receiving a delayed vaccination can be used to target future studies to assess their driving factors for delayed vaccination and barriers to vaccination in grades 5 and 6 and furthermore as a basis for designing and implementing tailored interventions if needed. Although determinants of non-timely HPV vaccination in Sweden have been assessed in another study (83), the findings of **study III** add further understanding of the importance of country of birth for the girl. The country of birth should be included as a determinant in addition to the parents' origin. The previous study, also identified a higher probability of HPV non-vaccination for parents having low income, educational level and parents with foreign background (83). The inequities in HPV vaccination identified in the studies warrants further studies of possible barriers in the NIP system to better understand the reason for the inequities. New insights may then be used for a tailored implementation of the NIP so that barriers may be avoided or minimized and equitable uptake can be achieved in the future. Lessons learned from using the TIP approach to address low MMR coverage can be useful if tailored interventions for HPV vaccination are needed.

Reflections of the TIP approach and implementation of tailored interventions

The TIP project launched in Sweden in 2013 was one of the first TIP approach pilots. Although at least 12 countries had used the TIP approach between 2013-2021, the project in Sweden is one of the first to go beyond the identification of barriers and drivers for suboptimal MMR uptake in a targeted population to the design and implementation of tailored strategies including elements of evaluation. A review of the TIP approach piloted in four countries, including Sweden, in 2016 stated that a strength of the TIP approach was the possibility to listen and understand individuals and communities from their perspectives and to be a diagnostic tool of value for the NIP (174). In Sweden, the TIP approach was proven to be a useful and valuable tool that guided the work stepwise and systematically to achieve an in-depth understanding of driving factors and barriers for MMR vaccination in the targeted community. The mapping of factors using the COM-B framework structured and clarified the barriers and driving factors for MMR vaccination for parents in the Somali community. In the years following the end of the implementation of the TIP project in 2017, a positive trend for the MMR vaccination uptake in the communities was noted. Additional evaluations of the vaccination coverage are still ongoing and will be presented and published once completed. Evidence-based tools to tailor and adapt the NIP when the uptake or vaccine acceptance is lower is essential. Without evaluation, guidance regarding helpful tools is lacking.

Tools and approaches to assess low uptake of vaccination are needed for the management and implementation of NIPs. This TIP project was the first exploration of locally low vaccination coverage by the PHAS involving a team at the unit for vaccination programs to gain experience in addressing vaccine acceptance by implementing tailored interventions. The experience is valuable as the management and implementation of the NIP need to find structured ways and tools to assess vaccination coverage from a vaccine acceptance point of view as well as equity. The TIP approach is one tool but others might be needed and more suitable depending on the aim and situation. Additional tools and approaches should be gathered to build a comprehensive toolbox for the management and implementation of the NIP. The TIP approach was flexible in terms of data collection from different sources and can either be scaled up or down depending on the resources. The lessons learned from TIP can support and help guide regional TIP initiatives and local implementation of tailored interventions when indicated. Therefore, the TIP approach has been translated into Swedish and is being piloted by four different regions in a regional and local context in close collaboration with the PHAS (110, 175).

Sustaining high vaccine acceptance and resilience for the NIP

The drop in HPV vaccination coverage of the first dose for girls born in 2004 (eligible for HPV vaccination in 2015) and the association of birth year to non-timely vaccination in **study III** coincided with the debate on the safety of the HPV vaccination in Denmark, 2014-2015. The coverage in Sweden, however, rebounded relatively quickly as the cohorts of 2005 resumed an uptake of 82% for HPV vaccination, which then increased for each subsequent cohort to 92% for girls born in 2010. At the time of the MMR controversy, a similar phenomenon of a temporary drop in the national MMR coverage in Sweden was seen, but it rebounded within a few years. The two events show that Sweden too can be affected and that, despite the very high vaccine acceptance shown in **studies I and II**, the country is not immune to changes in vaccine acceptance. New events, such as the safety scares for vaccinations, will happen in the future. As the history of vaccination reveals, vaccination has always been debated since the first smallpox vaccine was developed. Consequently, the management and implementation of the NIPs have to be ready and systematically assess vaccine acceptance on a recurring basis, particularly as it could facilitate the detection of signals and changes early. While many other countries experienced disruptions in vaccination programs during the covid-19 pandemic, the Swedish NIP showed resilience during the early period of the pandemic (176). Being able to withstand threats and disruptions to vaccine acceptance is a key aspect of sustaining resilient vaccination programs (177). Thus,

the exploring and understanding of factors for parental vaccine acceptance systematically in the Swedish context provides an important foundation to support the resilience of the NIP. As the vast majority of parents in Sweden currently choose to vaccinate their children, it is essential to find ways of keeping vaccine acceptance high for the future and thoroughly explore both drivers and challenges. This means not only focusing on parents with questions and concerns or on declining vaccinations. The driving factors of vaccine acceptance are just as important to understand and to promote in order to build resilience in the NIP. By conducting the studies that are included in this thesis, initial steps for the systematic assessment of parental vaccine acceptance to inform the NIP were taken. Continuation of the studies are needed to establish the assessment of parental vaccine acceptance on a recurring basis.

Methodological considerations

This thesis includes both qualitative and quantitative research methodologies, which strengthens it overall, as quantitative and qualitative methods jointly can provide a better understanding by adding different pieces (178). For this thesis, the mixed methods approach has enriched the understanding of parental vaccine acceptance in Sweden as the studies complemented one another to assess the overall aim from different angles and perspectives. An important strength of the qualitative studies is that parents and nurses were given an opportunity to share their experiences and perspectives in their own words and facilitate in-depth understandings from their point of view. The quantitative studies assessed factors for parental vaccine acceptance at a population level by using a survey and high-quality registries. Assessing factors for non-timely HPV vaccination by using registries with nearly 500,000 girls reflects the actual vaccination behavior for the outcome instead of relying on self-reported vaccination status and allows linkage to socioeconomic determinants of this outcome. Although non-timely vaccination was only assessed for the first dose and not two doses of HPV vaccination, it is still valuable for the public health as the WHO currently recommends either 1 or 2 doses of HPV vaccination, as one dose of vaccination provides protection against cancers. The strengths and limitations of the studies are discussed further in the subheadings below.

Validity

Validity in studies refers to how accurately the observed results reflect the true situation in the study population. The HPV registry-based study, **study III**, included close to 500,000 girls born in 2002-2010 and their respective parents in the study population, one of the largest studies conducted so far in Sweden, which gives much

power to the analyses. The unique personal identification number has allowed the linkage of national registries to obtain information about the girl and her parents for the specific study population.

There are limitations for each study in terms of selection bias. In **study III**, population-based registries were used to identify participants, which reduces the risk of selection bias. Some individuals were excluded, however, as individuals in Sweden who are not found in the registry could not be included in the study. To achieve better representativeness of the Swedish population, data was weighted to adjust for survey non-responders in **study I**. The use of a web panel and providing a survey in only Swedish, however, most likely excludes the participation of non-Swedish speaking parents in the population as well as newly immigrated individuals, who may also be a parental group underrepresented in attending CHCs. As the PHAS was the owner and in charge of both the panel and the survey, there might be possible bias in terms of social desirability and also underrepresentation of individuals not in favour of the PHAS and agencies. The groups and individuals who might be underrepresented in the study could have different attitudes toward vaccinations. In terms of information bias, both recall and social desirability bias are relevant to discuss. Information bias is decreased in **study III** as the outcome is assessed using NVR data. The data reflects the actual individual vaccination status and vaccination behavior instead of relying on self-reported vaccination status. In addition, the observed vaccination uptake is similar to the national statistics for vaccination coverage. Since the NVR was established in 2013, the reporting has been stable across the years. As the child's vaccination status was self-reported by the parents in **study I** and not verified by medical records, there could be a recall bias of parents not correctly remembering the vaccinations offered or received for the child. There are, however, similarities when comparing the vaccination status in the survey and the national vaccination coverage for childhood vaccines at the age of 2 years. In terms of the uptake for HPV, 89% of girls aged 11-15 years were fully vaccinated, according to the survey, whereas the national vaccination coverage for HPV was 81% for dose 1 in 2016. Vaccine hesitancy and lower acceptance could thus potentially be underestimated in the study as the study population differs from the Swedish population of parents to children in this age group. In **studies I** and **III**, the analyses were adjusted for potential confounders in logistic regressions. County of residency and birth year were considered potential confounders in **study III** as there might have been local differences in implementation or slight differences from one cohort to another. Thus, the variables were included in the adjusted final regression model, but some residual confounding is likely to remain. Other limitations include the income of people residing in Sweden but working abroad, which is lacking in the registry, as well as the use of birth dates of the girls and their corresponding school years to assume attendance in school. Although school is compulsory in Sweden until grade 9, no registries or data were used to assess actual school attendance. **Study I** was cross-sectional and thus, causality cannot be inferred and the results reflect a “snap-shot” of parental attitudes toward childhood

vaccinations at a particular point in time. The external validity and generalizability of the results of **studies I** and **III** should also be discussed. The generalizability of **study I** may be limited as vaccine acceptance is context-specific but of relevance for other settings and populations and if the context is deemed similar. The generalizability of the results of **study III** may be applicable to a larger extent in other settings, particularly in other high-income countries. Comparability and relevance for the variables included in the study have to be kept in mind when generalizing the study results.

Trustworthiness

The qualitative studies assessed parental vaccine acceptance and the experience of a tailored intervention from the perspective of nurses. The FGDs and in-depth interviews allowed them to express their views, beliefs and experiences in their own words. It is also important to acknowledge that the researcher, as an instrument for the data collection, will have an influence on the study as the researcher interacts with the participants in conducting the FGDs and interviews. In **study II**, an external consultant conducted the FGDs to represent a more neutral researcher instead of employees directly representing the PHAS. Having employees from PHAS ask questions directly to participants regarding the NIP may for instance, influence responses due to social desirability bias. The researchers at PHAS, however, developed the guide for the FGDs. For **study V**, two researchers who were also involved with the intervention design and implementation process conducted in-depth interviews. While their experiences may influence the data collection, their experiences also allowed them to ask detailed questions and use specific prompts for follow-up questions. An advantage of **study II** is the recruitment of participants by purposive sampling as a means to achieve variance in parents' background variables and thereby reflect potentially different perspectives and views. It is essential to discuss trustworthiness in relation to methodological considerations for qualitative research methods. Traditionally, trustworthiness is discussed in terms of credibility, transferability, dependability, and conformability (150, 179).

Credibility refers to the ability of the research to capture and measure what it aimed to examine. The equivalent of quantitative research methods is internal validity. The objectivity of the findings and neutrality of the data is reflected in *confirmability*, which means that findings should be based on the actual data and not due to bias and interpretations of the researcher. In **studies II, IV** and **V** the interdisciplinary research team has been valuable for the trustworthiness. In **studies II** and **V**, the transcripts were read several times and audio recordings were listened to for the researchers to be familiar with the data. Throughout the analytical process in all the qualitative studies, discussions were held among the research team and co-authors as peer-debriefing sessions to ensure the interpretations and findings were rooted in data and to decrease the bias of a single researcher. In **studies IV** and **V**, several of

the researchers were familiar with the community and culture over an extended period before the design and implementation of the intervention, which supports the credibility. In addition, the researchers had previous experience and expertise in qualitative methodology. **Studies I and II** both include parents to children and assess vaccine acceptance, which can be viewed as part of triangulation as they overlap in terms of target group and research topic, which supports the studies' credibility.

Dependability is the possibility of findings to be replicated if similar studies are conducted in similar contexts and target groups. To keep the focus and structure for the in-depth interviews and FGDs in **studies II and V**, a FGD guide and thematic guide were used to guide the data collection. In addition, the first interviews in **study V** were conducted jointly by two researchers so that similar data collection process could be used for the subsequent interviews conducted separately. **Study IV** describes the design and implementation of tailored interventions. By describing the process in detail, the dependability of the intervention project is strengthened by being transparent, which also allows others to assess the process and decisions made by the research teams of the information they had available at the time.

Transferability reflects the generalizability of the data to other contexts and populations. The journal publishing **study II**, BMC Public Health, required the submission of the qualitative manuscripts to include the “Consolidated criteria for reporting qualitative research” checklist (COREQ). The checklist can be a useful guide to describe research using interviews or FGDs comprehensively and thoroughly. The checklist is helpful for authors to be transparent about the settings and context, methods, findings, and interpretations. By thoroughly reporting qualitative research, readers can assess the quality of the research and its transferability. The detailed and transparent description of the intervention design and implementation in **study IV** allows the reader to assess the process and decide if it may be suitable to use in other contexts or populations. For the results in **studies IV and V**, it is important to keep in mind that they relate to a specific community and setting. Hence, generalizing the findings to other settings should be done with caution and inferred by the reader. Characteristics of parents participating in **study II** are lacking and should be included to enhance future studies.

Concluding remarks and future perspective

This thesis aims to provide an in-depth understanding of parental vaccine acceptance, particularly for HPV and MMR vaccinations. Results of the studies included in the thesis show that parents have confidence in vaccinations in the Swedish NIP, and both individual and societal factors were shown to be driving factors of parental vaccine acceptance. The vast majority of parents accept vaccination in the NIP for their children without any concerns. Despite the vaccine acceptance, challenges persist, particularly in relation to the HPV vaccination and also in terms of information regarding vaccinations. Proactive work is needed to sustain the current parental vaccine acceptance and high vaccine uptake in the future, as the situation can change quickly. The driving factors needs to be reinforced and promoted, while barriers needs to be addressed. Parents need to get their questions or concerns addressed in order to feel safe to make informed decisions. They should also receive adequate and sufficient information for their decision-making. Nurses have a key role in parental vaccine acceptance and their interaction with parents at the CHCs or school health platforms constitute a backbone of the Swedish NIP. Providing continued support and tools for nurses implementing the NIP is essential to facilitate their dialogue with parents and to enable informed parental decisions. The nurses play a vital role in the resilience of the NIP.

The inequities identified despite the implementation of HPV vaccination in a school-based system need to be further assessed to identify the barriers to non-timely vaccinations. Future studies should also assess the equity and social determinants relating to the other vaccinations included in the NIP. Additionally, the social determinants associated with getting a delayed HPV vaccination can be used to target future studies aiming to understand their driving factors and barriers to vaccinations and assess the role of maturity and decision-making without parental consent. Understanding the perspective of those girls might bring keys to tailoring the program for earlier acceptance of HPV vaccinations. Findings from future studies may enable the tailoring of the NIP and its implementation to decrease inequities. All children should have equal opportunity to be offered and vaccinated according to the NIP, regardless of their situation in relation to social determinants.

The aim of the thesis was also to gain experience in tailoring interventions to increase vaccine uptake. Two of the studies included in this thesis were based on the TIP approach which proved to be a valuable tool for understanding barriers to lower MMR vaccine uptake among parents in a Somali community. The approach provided a stepwise process and facilitated the design of evidence-informed intervention targeting nurses. According to the nurses, the dialogue with parents having low MMR vaccine acceptance was facilitated and enhanced following the tailored intervention. Future studies should also evaluate the tailored interventions designed and implemented for parents and to assess the MMR vaccination coverage within the studied community long-term. Evaluations of tools and interventions is important to identify effective interventions that can be used to address low vaccine uptake. The management and implementation of the NIP should have a toolbox at hand for addressing low vaccine uptake, for which the evidence-based TIP approach can be one of the tools.

The purpose of the studies was also to develop evidence-based methods to systematically inform the management and implementation of the NIP in Sweden regarding parental vaccine acceptance. The results demonstrate the value of using mixed methods of both quantitative and qualitative studies to provide different pieces of understanding for parental vaccine acceptance in relation to the NIP. Recurring assessment of parental vaccine acceptance should be part of the routine work to gain data for action to support the implementation of the NIP. The use of qualitative studies should not be underestimated as it can be powerful and valuable to listen to parents or health professionals describe their perspectives in their own words. No single study can capture all aspects of parental vaccine acceptance. Different studies with varying aims are needed to inform and provide data for action for the management and implementation of the NIP. Studies needed to support the management and implementation of the NIP may range from including a general population level, by geographical regions or specific vaccinations to subpopulations and contexts when indicated. The perspective of equity is important to consider and assess regularly so that immunization gaps due to social determinants can be reduced. In addition, studies focusing on nurses and health care professionals in the Swedish context are important as they have a key role in the NIP. Insights and results from studies are valuable in guiding support for the implementation of the NIP and in informing strategies for parental vaccine acceptance. This thesis is a starting point for establishing a systematic assessment of parental vaccine acceptance, including the perspective of equity, on a recurring basis. The best vaccines will only save lives and improve the health of children when parents accept the vaccinations.

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