Chapter 9

General discussion
Summary of the results

The European population is ageing. This will lead to an increase in the proportion of older adults. Consequently, taken into account the gradual deterioration of the immune system, the prevalence of infectious disease will rise among this population, leading to higher burden of disease and associated healthcare costs. Vaccination is one of the measures that might prevent part of this burden. This thesis aims to contribute to the body of work on the willingness of older adults (50 years and over) to accept vaccination. More specifically, it reveals vaccine preferences and acceptance rates for three vaccine candidates (pneumococcal disease, herpes zoster and pertussis vaccination). In addition, this thesis elaborates on the attitudes and intention of general practitioners towards vaccination for older adults. Such information is crucial to reach acceptance and successful implementation of vaccination aiming to contribute to healthy ageing.

In chapter 2, we identified three potential vaccine candidates that might complement the current influenza vaccination program. Based on information on the vaccine availability, the pathogen, disease outcomes and the cost effectiveness of vaccination, pneumococcal disease, herpes zoster and pertussis were selected. Chapter 3 describes a study that estimates the burden of the disease caused by these three infectious diseases in older adults. Influenza was also included. Pneumococcal disease caused the highest burden in older adults, due to the high mortality, followed by influenza, herpes zoster, and pertussis.

Using available literature, our next step was to identify key factors that influence the willingness to accept vaccination among older adults. Chapter 4 shows that the two most influential factors in the vaccination decision-making process among older adults are (negative) attitudes and beliefs about vaccination in general and beliefs about the vaccine characteristics (e.g., vaccination weakens someone’s immune system). Recommendations of healthcare workers and the individual’s perception of susceptibility to the targeted disease are also of high importance to older adults. The focus group study in chapter 5 shows that the risk of acquiring an infectious disease, vaccine characteristics, the severity and the implications of the infectious disease, previous vaccination experiences, and the general practitioner (GP), were all important in the Dutch older adults’ decision whether to accept vaccination or not. These key factors were mostly in line with international literature. While vaccinations were found to be important, questions were raised on the usefulness of vaccination at older age. This relates to, for example, the opinion to let nature run its course instead of trying to prevent something that is inevitable (death). Regarding the general practitioner; two active roles for the general practitioner were identified: leadership and an advisory role.

In chapter 6, using discrete choice experiments (DCE), high vaccine effectiveness, high mortality, and high vulnerability were identified as preferences for older adults when considering vaccination. These experiments showed that Dutch older adults preferred protection against the symptoms of pneumococcal disease over protection against the symptoms of influenza. Protection against influenza was preferred over
herpes zoster and pertussis. Regarding vaccine and disease characteristics, the number of vaccinations needed and the protection against the clinical syndrome of influenza were found more important to people aged 65 years and older than to people aged between 50 and 65 years. Vaccination acceptance rates for adults aged 50 years and older were estimated at 68% for pneumococcal disease, 58% for herpes zoster and 54% for pertussis vaccination. Estimated vaccination rates for persons aged 65 years and older were higher for all vaccinations than for persons aged between 50-65 years, for example 76% versus 58% for pneumococcal vaccination.

The two following studies focused on the attitude and intention of GPs towards expanding vaccination programs, since they have an important role for older adults considering vaccination (Chapter 7 and 8). Chapter 7 describes an interview study revealing that GPs do not necessarily have a positive attitude towards expanding the vaccination program of elderly. Gaining the most health benefits seems to be the most important reason to adhere to expanding vaccination programs. Other factors that matter to the GPs are the severity and the prevalence of the infectious disease. In addition, vaccination should be offered to high-risk groups. Chapter 8 describes a survey among GPs. In this study factors were identified that predicted intention of adults aged 60 years and over to accept vaccination against other diseases than influenza. Factors that had the highest predictive value were attitude towards offering additional vaccination other than influenza vaccination and towards vaccination as a preventive tool, the practical consideration of GPs being suitable to administer additional vaccination, and the attitude towards offering older people vaccination during an outbreak of an infectious disease.

A number of findings deserve to be highlighted in this discussion, as there is new literature or these findings came up across the different studies. Older adults seem to value the effectiveness of vaccines highly. From that perspective, it is relevant that recently, there have been developments in vaccine effectiveness for pneumococcal disease and herpes zoster vaccine. The results of the CAPITA study, a randomized controlled trial to determine the effectiveness of a 13-valent conjugated vaccine (Prevenar13) were published. The study showed a vaccine effectiveness around 45% in preventing community acquired pneumonia caused by a serotype included in the vaccine and non-bacteremic and non-invasive community-acquired pneumonia. For preventing invasive pneumococcal disease, a vaccine effectiveness of 75% was found. The CAPITA study also showed that the efficacy of the vaccine remained throughout the follow-up for almost 4 years (1). In our study (Chapter 6), we already accounted for a vaccine effectiveness of 50%, therefore this does not change the vaccination uptake estimate for pneumococcal disease.

For herpes zoster, a new vaccine is being developed but not yet available. This vaccine is an adjuvant herpes zoster subunit vaccine. Trials with this vaccine in persons aged 50 years and older showed a vaccine efficacy close to 97% for all age groups (50-59, 60-69, >70 years) (2). This eliminates the differences in vaccine effectiveness in different age-groups as described in the study of Oxman et. al (3). This new vaccine has
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to be given twice and no severe adverse events were attributed to the vaccine. In addition, it can also be given to immunocompromised patients for whom Zostavax is contra-indicated (2). These new results will influence the acceptance rate, as the current vaccine Zostavax has an effectiveness of around 50%. Using the model of our current discrete choice experiment, the estimated acceptance rate of this new vaccine would be 64% for persons aged 50 years and older instead of 52% with Zostavax³.

Chapter 4, 5 and 6 show that vulnerability to an infectious disease is a reoccurring theme, both among older adults as general practitioners. Vulnerability entails different entities such as perceived health status associated with age and co-morbidity, the risk of acquiring an infectious disease but also the more subjective self-reported health score. Feeling vulnerable was shown to lead to either a higher chance of accepting vaccination to protect oneself or a lower chance because people do not want to stress their body (even more). On the other hand, not feeling vulnerable could lead to either accepting vaccination to stay healthy or not accepting vaccination because one does not perceive any health threat by infectious diseases. In the choice experiment, self-reported health score was identified as a preference actor, meaning that people with a high self-reported health score in comparison to those with low reported health score attach more importance to: 1) vaccine that protects against high mortality infectious diseases 2) a vaccine with 100% effectiveness rate, and 3) a vaccine that has to be given twice. This also stresses the importance of the concept of vulnerability in the acceptance of vaccines in older adults.

Another interesting finding, that might be specifically true for the Dutch older adults, is that side effects of the vaccine hardly seem to play a role in the acceptation of vaccination. Whereas side effects are an important argument for Dutch parents to decline vaccination in children (4), Dutch older adults were found to be more indifferent and accept mild side effects as inevitable part of vaccination.

Methodological discussion

The overall aim of the studies presented in this thesis was to construct a generic model based on factors affecting the willingness to vaccinate to estimate the acceptance of vaccination against different vaccine preventable diseases among various age groups of elderly. With this model, vaccination acceptance could be estimated when implementing new vaccinations to the older adults. Even though the influenza vaccination is offered to persons aged 60 years and older, we chose to include persons aged 50 years and older as our study population. Vaccinating at this age means vaccinating before the immune system function declines and therefore may have biological advantages. Vaccinating at an earlier age may result in a stronger immune response and therefore better protection in later life (5). To anticipate future developments, we included this younger age group in our studies as well.

³The vaccine characteristics to estimate the acceptance of the new vaccine are 100% effectiveness and vaccinating twice. All the other remain the same as described in chapter six.
Questions could be raised about the studies that were conducted to select the attributes and levels to include in the discrete choice experiment (mainly chapter 4 and 5). Although the literature review offers an extensive overview of the factors related to vaccine uptake of older adults, including both quantitative and qualitative research, we have included articles in this study that were published over 20 years ago. Views on vaccination as well as public awareness have since changed. Doubts on relevance, however, are unwarranted, since no distinct differences in factors were identified in the older and newer articles. Regarding the focus group study, questions might be raised on the representativeness of the study population, because care home residents and men in general were underrepresented. In addition, the focus groups were held at a time when the media frequently presented reports on the role of the pharmaceutical industry in the debate about the provision of additional vaccines; we believe this media influence can be considered to be low since mistrust was not identified as a key theme in this study.

A particular strength of this study is its open explorative design allowing a wide range of factors to be identified. Taking into account the strengths and limitations, we feel confident that both the literature review and the focus group study form a solid foundation for the subsequent discrete choice study.

The interview and the survey performed among general practitioners might be weighed down by their sample sizes, making the studies prone to selection bias. For qualitative studies, the most important criteria to terminate the data collection is reaching saturation, which was reached in the interview study. Nonetheless, the participating GPs might have a particular interest either in research or in (elderly) vaccination, which should be taken into account when interpreting the study results. Nevertheless, we feel confident that these two studies are good starting points for exploring the attitudes and intentions of GP regarding vaccination of the elderly.

Regarding the responses collected during the discrete choice experiments, questions can be raised on the validity of this data. It has been mentioned (Chapter 6) that DCEs pose a cognitive burden on the participants. Although we have tried to circumvent this by simplifying the choice tasks as much as possible in the study design, it remains uncertain that respondents actually understood the tasks, even after a pilot study. From the literature, it appears that respondents, instead of using the information from the choice task, base their judgment mainly on their own experiences (possibly taking other factors not mentioned in the choice experiment into account) (6). As such, the respondents might not trade-off between attributes and levels of the scenarios in the DC tasks. For example, there could be a difference between reading and imagining the symptoms or experiencing the symptoms yourself. As a consequence, participants with and without prior disease experience may have interpreted the choice situations differently. Information about experienced sickness of the participants would therefore have been useful. This way, we might have identified a sub group of participants that had particular thoughts on vaccination since the different clinical symptoms were identified as significant factors determining vaccine (non)preferences.
Consequently, the coefficients may not reflect the trading off process that older adults engage in when deciding on vaccination. In addition, age has a significant effect on the consistency of completing the choice task, where older participants fail to answer consistently (7). A more recent study also shows that older adults might not trade-off between choices (8). Thus, concerns regarding the validity of discrete choice experiments exist.

Discrete choice experiments always reveal preferences of people based on hypothetical situations reflecting what they presumably would have chosen given the specific scenario. A possible solution to these concerns might be that respondents complete the questionnaire accompanied by a researcher, as suggested in the literature (8). These interviewers can answer questions and help respondents to interpret the attributes and levels and this way guide them through the questionnaire. This gives assurance that respondents interpret the DCE tasks appropriately and consequently, the validity of the data is ensured. However, the chance of introducing interviewer bias is present when using different interviewers.

Studies have shown that stated preferences could predict actual behavior. Recently, a study has been published investigating the predictive value of DCEs by comparing stated and revealed preferences among parents deciding whether or not to vaccinate their new born child against hepatitis B. It was found that 80% of the actual behavior was predicted by the stated preference DCE (9). It should also be mentioned that during our thinking out loud testing, the subjects of various ages found the choice tasks difficult but manageable. More importantly, the estimated vaccination rate of influenza for persons aged 65 years in our study is in line with the actual vaccination uptake in that same year. This supports face validity of the responses.

It is difficult to provide generic vaccine acceptance estimations based on the results described in this thesis, specifically the DCE results. The design of the DCE included specific clinical syndromes of the pertaining infectious diseases, consequently, the results might be vaccine-specific. However, the identified relative importance of the different disease and vaccine characteristics provide information on the acceptance of other vaccines than the three included vaccine candidates. For example, the vaccine acceptance will be higher for an infectious disease with high mortality than the vaccine acceptance of a vaccine that protects against an infectious disease with low mortality rates. Also, vaccine acceptance will be higher when vaccine effectiveness is high. This way, a rough estimation can be made on whether vaccines would be accepted in the older adult population. New developments for the current vaccine candidates can be incorporated as well. If a new vaccine is developed that has higher effectiveness, vaccine acceptance will probably increase.
Implications of this research

The estimated vaccine acceptance for the three vaccine candidates indicates that older adults are generally willing to accept vaccination. This implies that older adults would like to know about the available vaccines and therefore active communication on the availability of these vaccines should be initiated. This is independent of actually offering these vaccinations to older adults in a national program. These vaccines may be purchased yet they are not easy accessible. Older adults should have the opportunity to make an (informed) choice concerning their own healthy ageing through vaccination. After all, vaccination could provide health benefits as shown in chapter 2 and 3.

This thesis provides opportunities to develop communication strategies to inform older adults about these vaccines. First, it should be acknowledged that vaccine acceptance originates from attitudes, beliefs, and perceptions. Therefore, communication should focus on providing objective information to counter false beliefs and perceptions. Second, regarding the content of these communication messages, vaccine effectiveness, mortality rates and susceptibility rates were identified as highly relevant to older adults, therefore the information should focus on these aspects. This way, information can be tailored to the vaccine it concerns by focusing on the most important characteristics. The most apparent example for individual tailoring might be the perceived susceptibility and the actual susceptibility due to immunosenescence. Older adults do not feel at risk for infectious diseases while they in fact are. And feeling at risk is an important factor in accepting vaccination. Vaccine information should therefore convey the biological susceptibility of older adults.

In addition to the content of the communication messages, it should be taken into account that age-related views may exist so consequently, personalized information may be most required. These age-related views are reflected in vaccine preference and acceptances rates, the need for vaccination and the perceived severity of infectious diseases. This implies for example that for persons aged 50 to 65 years, it should be acknowledged that communication should also be focused on maintaining quality of life, while for persons aged 65 years and older, mortality is more important (chapter 6).

Finally yet importantly, this thesis also identifies the main sources for presenting the information to the public. It is clear that the GP plays an important role for older adults in the acceptance of a vaccine, more so than friends or family. Therefore, the GP seems to be the most suitable person to inform older adults on these vaccines and vaccination in general. However, chapter 5 shows that also in this case age-related views may exist. While older age group might be more submissive towards the GPs opinion, the younger age group consults the internet for information. This is important because these younger people are the ‘elderly of the future’. Special attention is needed to make sure that objective information is easily accessible on the Internet and actively offered by the GP’s or institutes like the RIVM to make people aware of the availability of this information. This could be done by spreading information pamphlets on the different vaccinations together with, for example, the invitation for the influenza vaccination. This means that persons aged 60 years and older will get a yearly reminder that other
vaccinations are also available and ensures that these people receive objective information. In addition, persons that come to the GP's office to get the influenza vaccination can also be actively offered information on other vaccinations by handing out information pamphlets.

This is in line with the finding that GP's see themselves as having an important role as advisor of older adults regarding vaccination. However, although chapter 7 shows that a positive attitude towards prevention in general and vaccination is present among GPs; a positive attitude towards offering older adults more vaccinations is not always obvious. For example, the infectious diseases focused on in this thesis were not found severe enough. GP's furthermore feel less need for younger people and/or healthy persons to be vaccinated. A risk assessment based on co-morbidity to identify risk groups in need of vaccination would be more in order. To obtain the cooperation of the GP's, the positive attitudes of GP's should be reinforced and the more negative attitudes should be countered. In chapter 8, it was shown that the attitude of GP's towards extra vaccination was largely predicted by perceptions on different disease characteristics. These perceptions should be either strengthened when these are correct or countered when these are incorrect with evidence based-information, which is also the preference of the GP's themselves. For example, supplementary training could be organized on this subject educating GP's not only on the different vaccines, but also on the willingness of older adults to facilitate the provision of information to the older adults even more.

Future research

Future research should focus on the eligibility of the proposed more tailored information provision and the impact of this information on the vaccine acceptance. For this, the influenza vaccination can be used. Using a randomized controlled design, one group of older adults would receive information focusing on the susceptibility for, and the mortality of influenza. Another group receives the current influenza vaccination information leaflet and a final group receives information on a totally different subject than vaccination. Then, all groups would be offered an influenza vaccination and differences in influenza vaccination uptake would be analyzed. They would also complete a questionnaire including questions on baseline characteristics to compare the groups, and questions on their intention and attitude towards vaccination as well as their opinion on the information provided. For years, there has been some debate concerning the influenza vaccination, therefore it would be best to present the choice sets in an unlabeled form (assigning non-labelled alternatives to the choice set, such as vaccine 1 and vaccine 2)

In addition, the theme of the usefulness of vaccination at older age has barely been touched upon and deserves a more detailed investigation. 'Is it not okay to get sick anymore' and 'you have to die of something' were some of the arguments of the older adults for rejecting vaccination. To study this further a more ethical and philosophical approach is required. In-depth-interviews with older adults and general practitioners could be conducted to specifically explore this aspect in more detail. And last, this thesis
only scratches the surface of attitudes of GP’s regarding expanding older adult vaccination so more in depth research is necessary to understand the viewpoints of the GP’s. One interesting idea would be to conduct a choice experiment among GP’s to compare their vaccines preferences with the preferences of older adults.

And last, if the availability of the more vaccines will be more actively announced, research should focus on the practical implications of this. This concerns for example equality in obtaining vaccines and other logistics.

Expanded vaccination programs in other countries

To date, influenza vaccination is by far the most offered vaccination to elderly in Europe. In The Netherlands it is the only vaccination routinely offered to persons 60 years and older currently. In this thesis, pneumococcal, herpes zoster and pertussis were identified as vaccine candidates and vaccine acceptance for these vaccines was estimated. In other European countries, these vaccines are already offered or recommended to (older) adults. In addition, national vaccination programs are organized for pneumococcal vaccination and herpes zoster vaccination in the United Kingdom and the United States of America.

In Germany, Austria and France, for example, a combined vaccination of Diphtheria, tetanus and pertussis every 5-10 years in adult life is recommended and funded. Herpes zoster vaccination is recommended (but not funded) in Austria and Czech Republic for persons aged 50 years and older. In France and The United Kingdom, this vaccination is recommended and funded for people aged 65 and older, and 70 and older, respectively.. For pneumococcal disease, several forms of recommendations (co-morbidity, catch-up, general recommendation) exist in Europe, including several European countries (10).

The national pneumococcal vaccination program in the United Kingdom started in August 2013. This program offers pneumococcal vaccination to adults over 65 years and adults aged between 20-64 years who have been defined as a risk group (11). The vaccine used in the UK is the 23-valent pneumococcal polysaccharide vaccine (known as PPV23). The vaccine is given once with no annually repetitions except for individuals with no spleen, splenic dysfunction or chronic renal disease who will require boosters at five year intervals. The GPs are invited to implement the immunization program and upon acceptance, the attending GP will also conduct the influenza vaccination program. The GP’s office collects data on vaccine acceptance and refusal (12). Vaccination coverage (percentage of eligible elderly that received the vaccination) has remain stable over the last years, around 68% (13).

In September of 2013, The United Kingdom were the first European country to implement a national immunization herpes zoster vaccination program, offering herpes zoster vaccination to all elderly of 70 years and older and catch up vaccination to elderly of 78 years and older. The elderly are invited by their GP’s to receive the herpes zoster vaccination when they become eligible (12,14). After the implementation of the immunization program, vaccine uptake rates were 61.8% in the first year and 55.3% in the second year. Less than 10% of the eligible elderly actively declined the vaccination.
Now, in its third year, a vaccine coverage of 46% is achieved thus far (16). This might have to do with the changing health service in the United Kingdom, as an increasing number of private providers might lead to an increase in the mistrust of the public in vaccination campaigns (17).

Beyond European borders, the United States implemented a herpes zoster vaccination program in 2007 for adults aged 60 years and older. In 2007, a vaccination uptake of 1.9% was estimated but this steadily increased to 27.1% in 2014 (18,19). In 2014, pneumococcal vaccination was recommended for all adults aged 65 years and older. The vaccination uptake for adults aged 65 and older was 61.3% in 2014 for pneumococcal conjugate vaccine 13 (PCV 13) (19).

Comparing our estimated vaccination rates to the uptake in the discussed countries, our estimates are higher. For pneumococcal disease, our estimated vaccination rate for persons aged 65 years and older is 76.2% compared to 61.3% in the United States and 68% in the United Kingdom. The same is the case for herpes zoster vaccination; 68% versus 27% in United States and 46% in the United Kingdom. This suggests that our estimates might be too high, but a comparison of influenza vaccination rates between the United Kingdom and the Netherlands shows that vaccination uptake can also be higher in the United Kingdom (71% vs 65% in the Netherlands) (10,20).

In the Netherlands, the Health Council of the Netherlands has published her advice regarding herpes zoster vaccination and came to the conclusion that routine vaccination of elderly with the currently available vaccine(s) is not warranted. Reasons for this were that shingles does not pose a threat to society and the vaccine effectiveness and duration of protection were deemed insufficient. Should the new vaccine (discussed earlier) get market authorization and show high efficacy, the advice of the Health Council may be reconsidered (21). The Health Council of the Netherlands currently debates vaccination against pneumococcal disease for the elderly. Pertussis vaccination for older adults is currently not a priority. For the influenza vaccination, the most recent updates on the vaccine uptake show that acceptance is decreasing in the age group of persons aged 60-64 years old. This has been the case for several years now (20). Looking at the results of our studies, this might be because these older adults do not feel vulnerable for influenza.

Healthy Ageing and vaccination: challenges remaining

Considering vaccination as a measure to contribute to ‘Healthy Ageing’ poses more challenges than the acceptance of this measure. First, there is the clinical or biological aspect of vaccinating elderly. The immunosenescence which has been discussed several times in this thesis does not only lead to an increased vulnerability to infectious disease, it has consequences for the immune response induced by vaccines. It affects both innate and adaptive immunity, limiting the response to pathogens and to vaccines (22). For example, in children, a vaccine effectiveness of 90% or higher is common, while the vaccine effectiveness in elderly is more commonly around 50%. This reduced
effectiveness is especially important since older adults’ value vaccine effectiveness highly. In addition, elderly are a more frail population, often being excluded from clinical trials testing new vaccines. This leads to a lack of evidence to inform immunization policy for this growing demographic group (23). More vaccination studies, looking specifically at this subgroup of the population might therefore be relevant.

Besides the lack of knowledge, a paradigm shift might be required as suggested by Macntyre. The waning efficacy of vaccines should be considered in the light of the increasing disease incidence. In other words, if a vaccine is 50% effective, it still prevents 50% of the disease cases (23). And what is the relevance of reduced vaccine efficacy if levels of protection drop only after 10 years when life-expectancy is also 10 years? The focus on preventing disease completely might therefore be not realistic and a shift in focus reducing early mortality and morbidity might be required.

General conclusion

This thesis gives insights into the willingness of older adults to receive vaccination. It is apparent that the decision of older adults to accept vaccination is not based on a single argument but on multiple arguments. Most certainly, a part of the older adult population will base their decision mostly on the opinion of the GP. However, the rest will weigh the pros and cons, taking their perceived vulnerability, the vaccine effectiveness and severity of the infectious disease into account. Overall, older adults are willing to accept vaccination. Considering the studies in this thesis, pneumococcal vaccination will be the vaccination with the highest acceptance. Herpes vaccination follows in second place and pertussis in last place. However, this thesis also shows that individual differences exist in accepting vaccination. These differences are most apparent when looking at the age of the older adults, their influenza vaccination status and their self-perceived health. Therefore, it is of the utmost importance to focus on tailored information when implementing new vaccines to achieve the highest vaccination uptake possible in an effort to contribute to healthy ageing.
References


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