Chapter 1

General introduction
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History of vaccination

Vaccines have been very successful in preventing infectious diseases. Since the implementation of routine vaccination of children, the incidence of childhood disease and mortality has reduced significantly (1). Vaccination has a long history. In the 7th century, Indian Buddhists drank snake venom in an attempt to become immune to its effect (2). The work of Edward Jenner in the 18th century represents the first scientific attempt to control an infectious disease by the deliberate use of vaccination, which created the basis for the development of the current immunization practices (3). Jenner demonstrated that inoculation with pus from cowpox protected against smallpox, a serious disease which caused 400,000 deaths per year in Europe in the 18th century (2).

In the 19th century, more vaccines were developed. Louis Pasteur was the first to develop attenuated viral and bacterial vaccines (4). His research resulted in a breakthrough in the prevention of infectious diseases by establishing the basis of vaccinology, which is founded on the principle of isolation, inactivation, and administration of disease causing pathogens. In developed countries, national immunization programs have drastically reduced the incidence of many of the viral and bacterial infections that traditionally affected children. Vaccination has played a key role in the eradication of smallpox in 1979 and this was the first great success in global infectious disease control.

In the Netherlands, the National Immunization Program (NIP) started in 1957. At the onset of the program, children were routinely offered vaccination on a voluntary basis against diphtheria, tetanus, pertussis, and poliomyelitis. Over the years, this program developed into a general vaccination program for children with vaccinations scheduled between the ages of two months and 12 years (5). Currently, this vaccination program entails vaccination against diphtheria, tetanus, pertussis, polio, measles, mumps, rubella, meningococcal disease type C, Haemophilus influenza type B (Hib) hepatitis B, pneumococcal disease, and human papillomavirus. In the Netherlands, participation in this program is high (around 95%), resulting in low incidences of most diseases included in the NIP (6).

New target groups for vaccinations and criteria for expanding vaccination programs

Forty years after the introduction of the Dutch NIP for children, a new target population for vaccination received increased attention in the Netherlands. In 1997, the National Influenza Prevention Program was implemented, offering influenza vaccination to persons aged 65 years and older and certain other risk groups to prevent associated complications and mortality of influenza (7). Influenza vaccination is offered on a voluntarily basis. Other European countries recommended influenza vaccination to their older citizens as well. Between 1997 and 2007, vaccination uptake in the Netherlands was estimated to be around 74%, almost reaching the target set by the World Health
Organization of 75% (8). Uptake of influenza vaccination in the Netherlands was the highest in Europe (9).

In 2007, the age threshold for influenza vaccination was lowered to 60 years because influenza vaccination was also considered cost-effective for this population (7). From 2007 onwards, acceptance of the influenza vaccine gradually decreased to 65.7% in 2013 (8). In response to discussions regarding vaccination against influenza of healthy elderly aged 60 years and older, the Health Council (Gezondheidsraad) concluded in her advice in 2014 that there is sufficient evidence that influenza vaccination offers protection against influenza and its complications in this age group (10).

Also in 2007, the Health Council of the Netherlands introduced a ‘vaccination throughout life’-concept and identified older adults in general as a target group for expanding vaccination. At that time, several new vaccines had become available to protect against diseases prevalent in the older age groups such as pneumococcal and herpes zoster (11). However, none of these vaccines were part of a routine vaccination program in the Netherlands. In 2013, awareness on the underutilization of these available and registered vaccines was raised as their increased uptake may unlock further potential health benefits. The Health Council of the Netherlands concluded that a single assessment framework should be used to assess all vaccinations for implementation to improve the organization of vaccination care and make registered vaccines more accessible for all ages (12).

The need for vaccination of the elderly

The potential health benefits of vaccination among the older adult population become even more important with the shifting global demography and ageing of populations worldwide. The prognosis is that the median age of the world population increases from 26.6 years in 2000 to 45.6 years by 2100 (13). For the Netherlands specifically, by 2040, 26% of the Dutch population will be aged 65 years and older, compared to 16% in 2012. Of this group, two million people will be 80 years or older by 2055 (14). Age-related conditions such as immunosenescence (the gradual deterioration of the immune system), general frailty and the potential presence of co-morbidity are projected to result in up to 3500 fatalities a year due to infectious diseases and a strong increase in hospital admissions among persons aged 65 years old by 2040 (15). Vaccinating against infectious diseases other than influenza could reduce this burden of disease and therefore contribute to healthy ageing and reducing healthcare costs.

Currently, healthcare costs rise steeply with age and are highest for the very old, translating into 45,000 euro per capita for people aged 95 and older for the year 2007. Over the period 1999-2010, general healthcare expenditures have risen 7.2% per year. The estimation is that about 15% of this rise can be attributed to ageing. In 2007, 1.4% of the costs of the healthcare was the result of infectious diseases and parasitic diseases. Almost 50% of these costs were incurred by persons aged 45 years and older. However, respiratory infections such as influenza and pneumonia were not included in this
General introduction

calculation, causing an underestimation of the healthcare costs for this group of infectious diseases (16).

Introducing or adapting any vaccination program must be supported by scientific evidence. The Health Council of the Netherlands composed an assessment framework of seven criteria (Table 1) to decide whether, based on the available scientific evidence, vaccination is justified (11).

Table 1: The 7 criteria of the assessment framework to decide on the implementation of new vaccines.

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<td>1. The infectious disease causes considerable disease burden within the population.</td>
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<td>2. Vaccination may be expected to considerably reduce the disease burden within the population.</td>
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<td>3. Any adverse reactions associated with vaccination are not sufficient to substantially diminish the public health benefit.</td>
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<td>4. The inconvenience or discomfort that an individual may be expected to experience in connection with his/her personal vaccination is not disproportionate in relation to the health benefit for the individual concerned and the population as a whole.</td>
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<tr>
<td>5. The inconvenience or discomfort that an individual may be expected to experience in connection with the vaccination program as a whole is not disproportionate in relation to the health benefit for the individual concerned and the population as a whole.</td>
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<td>6. The ratio between the cost of vaccination and the associated health benefit compares favorably to the cost-benefit ratio associated with other means of reducing the relevant disease burden.</td>
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<td>7. The provision of vaccination may be expected to serve an urgent or potentially urgent public health need.</td>
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Influenza vaccination and other preventive strategies in older adults

In the Netherlands, the Dutch Ministry of Health, Welfare and Sport decides which risk groups are eligible for the National Influenza Prevention Program, as advised by the Health Council of the Netherlands. The general practitioner’s office is the central location for organizing these immunization campaigns and the general practitioner (together with the practice nurse) selects, invites, and vaccinates the target population, accounting for 95% of all vaccinations administered to risk groups (18).
Vaccination is part of (disease) prevention. However, it is not the only type of prevention that is implemented for older adults in the Netherlands. Over the years, prevention has become more important in the Dutch national healthcare. The aim of these preventive interventions is to keep elderly independent, autonomous and healthy for as long as possible, thereby achieving healthy ageing (19). Examples of prevention programs other than the influenza vaccination program implemented in the Netherlands concern breast cancer screening, fall prevention programs, prevention programs to prevent loneliness, pressure ulcers prevention, healthy diet and general health check-ups (20).

Aim of this thesis

Recent pleas for older adult vaccination have been published, summarizing the benefits of an extended adult vaccination program (21,22). In order for vaccination in older adults to be as successful as childhood vaccination, a crucial factor is the acceptance of this way of prevention. This is emphasized by the decrease of the influenza vaccination uptake. The aim of this thesis is to identify prominent factors that play a role in the vaccination accepting process. We devised an experiment in order to determine the relative importance of these identified factors. The ultimate goal was to build a model that would be able to predict the willingness to accept vaccination against different vaccine preventable diseases among various age-groups of older adults (50 years and older).

Dissertation outline

We first updated the scientific evidence regarding other vaccinations than influenza to older adults using the evaluation model of Kimman (Chapter 2). Vaccines included in this review were herpes zoster, pneumococcal disease, pertussis, and hepatitis A vaccination. In Chapter 3, we present a disease burden study among older adults regarding influenza, pneumococcal disease, herpes zoster, and pertussis. In this study Disability-Adjusted Life Years (DALYs) were calculated for each of the four infectious diseases for the older adult population to compare the burden of disease.

Chapter 4 and 5 address the relevant determinants for older adults to accept vaccination. In Chapter 4, a literature review is presented to identify potential factors important in the vaccination evaluation process in the international literature. Chapter 5 describes a focus group study performed with Dutch older adults aiming to identify determinants of vaccine acceptance relevant for the elderly Dutch population. Chapter 6 describes a discrete choice experiment that was conducted based on the information from chapter 4 and 5 to determine the relative importance between the most important determinants.

This thesis focusses on the older adults and their considerations for (and against) vaccination. Yet, it is known that the general practitioner (GP) and particularly the message they convey as professionals plays an important role in the vaccination process...
General introduction

of older adults. Notably, as medical professionals they currently act as (responsible) administrator of the influenza vaccination in several countries. Therefore, we conducted an interview study (Chapter 7) that explores the attitudes and intention of GPs towards vaccination of older adults in general as well the possible implementation of more vaccines. In chapter 8, we conducted a survey among Dutch GP’s to quantify the results found in the chapter 7. Finally, Chapter 9 summarizes the major findings of the studies and the practical implications of the results are discussed, as well as challenges that remain. Finally, suggestions for future research are presented.
References


