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REASONS FOR NON-VACCINATION

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The words of Jerome K. Jerome (1859-1927):
"It is impossible to enjoy idling thoroughly unless one has plenty to do."

I agree but now its time for an idling summer holiday!

Eva Dannetun
Sunday, May 7th, 2006

ABSTRACT

Vaccines are among the most effective public health interventions used today. Population based vaccination programmes are mainly aimed at protecting children against common childhood diseases, but other population groups are also the targets for different recommendations. The objectives of this thesis were to assess coverage and reasons for non-vaccination for three of vaccination programmes recommended by the National Board of Health and Welfare: influenza vaccine for the elderly, measles-mumps-rubella vaccine (MMR) for children and hepatitis B vaccine for health-care workers, and also to assess parental knowledge and attitudes towards hepatitis B vaccine for their children.

We found that even a well-established and functioning surveillance system on childhood vaccinations cannot present all data needed to fully evaluate the programme. The current national system overestimates the coverage for MMR among 2-year-olds and fails to record delayed vaccinations. Our studies show that relatively easy and inexpensive methods can supply information to complement available data. For vaccination programmes such as influenza for the elderly and hepatitis B for health-care workers there are scarce data available, and the use of focused studies may be the only option to evaluate the programmes. By conducting face-to-face interviews we found that coverage for influenza vaccination in an identified risk group (65+) was only 30%. A point prevalence survey among health-care workers showed that only half of those who had started a vaccination course of hepatitis B vaccine had actually completed it – despite the fact that the majority of them experienced a risk of exposure once a week or more often. The results show that improvements can be made and repeated studies could be used to evaluate measures taken.

Focused studies provide the only option when studying knowledge, attitudes and practice regarding both existing and future vaccination programmes. These can be time-consuming and new ways of collecting data could be an asset. However, despite a favourable situation with high access to the Internet and a target group of the appropriate age, our studies showed that web-based questionnaires still yield significantly lower response rates than the “classical” mailed paper questionnaire.

When studying reasons for non-vaccination, we found a clear lack of knowledge among target groups. We also found that the most important channel to inform them is via health-care staff. Parents of children who should receive MMR, elderly who should receive influenza vaccine, and health-care workers who should receive hepatitis B vaccine all need a chance to discuss their concerns such as necessity of the vaccine, fear of side-effects, etc., with well-informed health-care staff when deciding whether or not to get vaccinated. Health professionals play an important role in the implementation of the nationally recommended vaccinations. Information and advice from well-educated doctors and nurses is positively associated with vaccination. This role should be strengthened and ways to avoid missed opportunities should be further explored. It is also clear that non-vaccination is mostly a question of people not being made aware or reminded of the benefits of vaccines, and systems to provide automatic reminders should be developed.

Keywords: Vaccination coverage, influenza, MMR, hepatitis B, self reported data, elderly, childhood vaccinations, health-care workers, parents' attitudes, paper, web questionnaire.

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SVENSK SAMMANFATTNING

Vaccination mot infektionssjukdomar är en av de mest framgångsrika preventiva folkhälsoåtgärderna som utvecklats. I ett befolkningsperspektiv har vaccinationer betydelse både för den enskilde individen och för samhället som helhet. Populationsbaserade vaccinationsprogram är oftast inriktade på barnvaccinationer men det finns även andra grupper i befolkningen som berörs av generella vaccinationsrekommendationer.

Syftet med detta avhandlingsarbete har varit att;
- ta reda på andelen vaccinerade och orsaker till eventuell utebliven vaccination för tre nationella vaccinationsprogram;
    - influensavaccination för personer som är 65 år och äldre,
    - mässling, påssjuka och röda hund, MPR vaccination, för barn vid 18 månaders ålder
    - hepatit B vaccination för sjukvårdspersonal med frekvent blodkontakt.
- Ett ytterligare syfte var att undersöka föräldrars kunskap om sjukdomen hepatit B och inställning till ett eventuellt erbjudande att vaccinera sitt barn mot denna sjukdom.

Vi fann att även det väl etablerade och väl fungerande rapporteringssystemet för barnvaccinationsprogrammet inte kan presentera all nödvändiga data som behövs för att helt utvärdera programmet. Det befintliga systemet överskattar täckningsgraden för MPR hos tvååringar och missar om vaccinationen ges vid senare tillfälle. Vi fann att vår studie som genomfördes med en relativt enkel och förhållandevis billig metod kunde bidra med värdefull information som komplement till det befintliga systemets data. För vaccinationsprogram som t.ex. det för influensavaccination av de äldre och hepatit B vaccination för sjukvårdspersonal, finns endast sporadisk data tillgängliga. I dessa fall är riktade studier enda möjligheten att utvärdera hur väl dessa rekommendationer efterlevs. Genom att intervjua slumpmässigt utvalda personer som var 65 år eller äldre, och följaktligen borde vara vaccinerade mot influensa fann vi att vaccinationstäckningen var låg, endast 30%. I en punktprevalensstudie där vaccination mot hepatit B bland sjukvårdsanställda undersöktes fann vi att av dem som påbörjade vaccinationsschemat var det endast hälften som fullföljde. Detta trots att majoriteten minst en gång i veckan upplevde sig vara utsatt för risk för blodsmitta i sitt arbete. Resultaten visar att förbättringar kan göras och upprepade studier kan användas för att mäta effekten av vidtagna åtgärder.

Riktade undersökningar är det enda möjliga alternativet vid studier av kunskap, attityd och handlande för både befintliga och framtida vaccinationsprogram. Många av de möjliga metoderna är tidskrävande och nya sätt att samla data bör utforskas. I studien om föräldrars attityder till hepatit B vaccin för barn, jämfördes även svarsfrekvensen mellan en pappers- och en webbversion av enkäten. Trots en fördelaktig situation med stor tillgång till Internet och en målgrupp i passande ålder visar våra resultat att det webbaserade frågeformuläret gav signifikant lägre respons än den ”klassiska” postenkäten.

Resultaten från undersökningarna av orsaker till utebliven vaccination visar tydligt att kunskaperna om de riktade vaccinationsrekommendationerna inte har nått ut till den det berör. Vi fann också att den viktigaste informationskanalen för att nå ut är sjukvårdspersonal. Föräldrar som ska låta vaccinera sitt barn med MPR, den äldre som ska vaccineras mot influensa och sjukvårdspersonal som ska ha hepatit B vaccin behöver alla få en chans att diskutera sina frågor, såsom oro för biverkningar och fördelar med immunisering, med en välutbildad vaccinationskunnig person. Sjukvårdspersonalen spelar en viktig roll för implementering av de nationella rekommendationerna för vaccination. Information och rådgivning från välutbildade läkare och sjuksköterskor är positivt associerat med utförd vaccination. Denna viktiga roll bör stärkas, sätt att undvika missade vaccinationstillfällen bör utforskas vidare och ett system som automatiskt ger en påminnelse borde utvecklas.

LIST OF PUBLICATIONS

This thesis is based on the following papers:

I. Dannetun E, Tegnell A, Normann B, Garpenholt Ö, Giesecke J. Influenza vaccine coverage and reasons for non-vaccination in a sample of people above 65 years of age, in Sweden, 1998 – 2000.
Scand J Infect Dis 2003; 35: 389-393.

II. Dannetun E, Tegnell A, Hermansson G, Törner A, Giesecke J. Timeliness of MMR vaccination – influence on vaccination coverage.
Vaccine 2004; 22: 4228-4232

III. Dannetun E, Tegnell A, Törner A, Giesecke J. Coverage of hepatitis B vaccination in Swedish healthcare workers.
J Hosp Infect 2006; 63:201-204.

IV. Dannetun E, Tegnell A, Giesecke J. Parents' attitudes towards hepatitis B vaccination for their children. A survey comparing paper-, and web questionnaires, Sweden 2005.
Submitted

CONTENTS

LIST OF ABBREVIATIONS

CHC	Child Health Centre
EPI	Expanded programme for immunization
GP	General practitioner
HBsAg	Hepatitis B surface antigen
HCW	Health-care worker
MMR	Measles, mumps and rubella vaccine
NBHW	National Board of Health and Welfare
NCDS	National Communicable Disease System
NPV	Negative predictive value
SCB	Statistics Sweden
SHC	School Health Centre
SME	County Department for Communicable Disease Control
SMI	The Swedish Institute for Infection Disease Control
SML	Swedish Communicable Disease Act (2004)
WBC	Well Baby Clinic (the same as CHC above)
WHO	World Health Organization

INTRODUCTION

Immunization is a cornerstone of preventive medicine, and with the exception of safe water no other modality has had such a major effect on morbidity and mortality reduction.[1] The word vaccine derives from vacca, which is Latin for cow. In the late eighteenth century, the English country-side physician Edward Jenner noticed that women who milked cows and who got infected with cowpox on their hands from sore cow teats seemed to be protected against smallpox. To test the theory that having had cowpox was protective against smallpox he inoculated an eight-year old boy with the contents of cowpox vesicles on the 14 of May 1796. Six weeks later the boy was once again inoculated, this time with the contents from smallpox pus. The results were triumphant: the boy showed no signs of disease. This was a new and a safer method compared to the inoculation with smallpox pus that was the preferred method prior to Jenner's. The vaccination procedure evolved and less than two centuries later the smallpox virus and the disease were eradicated, and this vaccination could be stopped.

Since Jenner's “first” vaccination many vaccines have been developed but the principle is still the same. By exposing subjects to some modified form of the infectious agent, the immune system is triggered to respond to the antigen and produce protection against the disease. There are a large number of different vaccine types and vaccine products to be considered, and vaccinology has become an advanced science building on immunology and microbiology, medical knowledge about disease and prevention, surveillance of vaccine preventable diseases, epidemiology, and more.

VACCINATION PROGRAMME

The objective of a vaccination programme is to gain control of, or even better eradicate the disease for which the offered immunizations are effective. Not all vaccine-preventable diseases are possible to eradicate by vaccine alone: in principle this is only possible for diseases caused by microorganism were man is the sole host. So fare smallpox is the only disease that has been successfully eradicated.

Recommendations in a general vaccination programmes are often given with intent to provide protection both for the immunized individual and for the population as a whole. To reach this goal, the vaccination programme stipulates at what age and at what time interval the different vaccines should be administered. In the majority of countries, there exist general vaccine recommendations that cover the entire population. The more individuals that are successfully vaccinated against an infectious disease, the higher the level of immune individuals will be in the population. And as a consequence of this there will be fewer susceptible individuals that can spread the infection. If enough individuals are immunized, the risk of exposure of the still un-vaccinated will decrease to a point where epidemics can no longer be sustained, and the disease will stop circulating even if there remain susceptible individuals in the population.[2] This effect is called “herd immunity” and when this coverage level is reached even children who have not yet been vaccinated - such as newborns or children that for some reason cannot be vaccinated - will still be protected.

The coverage level necessary to attain herd immunity depends on three factors: the transmissibility of the disease, the contact pattern in the society in which the diseases is spreading, and the duration of infectivity in an infected person.[3] The precise level of population immunity at which transmission of a highly infectious disease like measles is interrupted is not known, but seroprevalence studies in developed countries with and without endemic measles transmission suggest that it is the range of 90–95%.[4]

When herd immunity level has been achieved, importation of for example measles results in only sporadic cases or in small clusters.[5] The positive effect of herd immunity can thus be achieved through well implemented, and maintained general vaccination programmes.

TARGETED PROGRAMMES

When the overall incidence in the population of a vaccine preventable disease is low, the vaccine is often not offered as a general programme. Instead protection may be targeted at those at higher risk of exposure or of severe disease. Examples of such targeted programmes in Sweden are vaccinations against tuberculosis, hepatitis B, and influenza.

Surveillance

There are several reasons for measuring vaccination coverage. The most obvious is to evaluate the effectiveness of immunization programmes, but this evaluation is also generating data for feedback to health-care professionals who administer the vaccinations as well as for decision makers. Another important reason is to identify areas of low coverage.

There are different ways to assess coverage: a rapid way is by collecting data on the number of distributed doses of vaccine in an area and relating this to numbers of possible vaccinees in the same region. This method is only suitable when distribution of vaccines is done from one or a few distributors, and when population data is attainable. These data can give a rough coverage estimate, but they give no information on how many doses were actually administered, nor who were the recipients and at what age they where vaccinated.

Another method of assessing effectiveness of a large-scale vaccination programme is by observing the effect that the introduction of the vaccine has on the incidence of the disease in question. Vaccines that are successfully introduced can have a dramatic effect on this incidence. This surveillance requires accurate registration of number of clinical as well as laboratory-verified cases. It yields long-term incidence trends, and is routinely used in many countries.[6, 7]

Annual systematic collection of data is also performed in most developed countries to calculate the percentage of children vaccinated. These data are reported on a national level for children at the age of two on an annual basis, and also forwarded to the World Health organization, WHO, where such data from most of the 192 member countries are collected and reported. These data can be retrieved on www.who.int.

Another method of assessing population immunity against a vaccine preventable disease is through cross-sectional seroprevalence studies that measure the levels of antibodies against one or more of the antigens in the vaccine in a sample of the population. Such serological surveys are used to evaluate vaccine efficacy, and also to follow the waning immune response to a vaccination over time.[8-10]

Coverage assessment by using samples from the population can be done in different ways: cluster, random sampling, or systematic collection. Cluster sampling is a method to assess coverage established by the WHO expanded programme for immunization, EPI. The method involves a two-stage sampling. First the type of cluster to be used - e.g., school, village, etc. - is decided on, and then a random selection of 30 of these clusters are sampled within the investigated geographic area. In the second stage 7 individuals are randomly selected from each cluster and their vaccination status assessed. From these 210 individuals the proportion of vaccinated individuals in the area can be estimated. This method allows for very rapid assessments: if 30 persons each interview seven subjects at 30 different locations, using a structured questionnaire, data could be collected in one day. And by entering the data into a computerized statistical program, results can be attained within days. With a sample size of 210 subjects the cluster sampling method gives a 95% confidence interval around the estimated proportion vaccinated of some ± 5-10 percentage units.[11]

Random sampling methods are commonly used when gathering information on coverage and attitudes to vaccines. Samples can be drawn from available registers, and data on self-reported vaccination status or attitudes to vaccination may be collected in direct face-to-face or telephone interviews,[12-15] or by distributing paper questionnaires.[16-19]

THE SWEDISH HEALTH-CARE SYSTEM

An important role for central government is to establish the principles for health services through laws and ordinances established by the parliament. The two most important Swedish acts for vaccination issues are the Health and Medical Service Act of 1982 and the Swedish Communicable Disease Act of 2004 (SML). The National Board of Health and Welfare, NBHW, is the central advisory and supervisory agency for public health. The NBHW has responsibility to issue national guidelines as well as to follow up and ascertain that services provided correspond to the goals laid down by the central government.

The Swedish Institute for Infectious Disease Control (SMI) is a government expert authority with a mission to monitor the epidemiology of infectious diseases among Swedish citizens and promote control and prevention of these diseases. Surveillance data on the 58 notifiable diseases in the SML act and coverage for the vaccines in the recommended childhood vaccination programme are gathered from the county councils. Data are analyzed and compiled on a national as well as on a regional level by the SMI, and presented annually. Serological cross-sectional studies from representative samples of the Swedish population have repeatedly been undertaken by the SMI. This was first done in 1960, and in more resent years such surveys were performed in 1990-1991 and in 1997. These studies have generated valuable

information on antibody response and serological immunity.[20-24] Plans are currently under development for a new serological survey to be performed in 2007 (personal communication Rose-Marie Carlsson, SMI).

The county council is responsible for providing health services and achieving a high standard of public health. Sweden is divided into twenty-one county councils. The county councils levies taxes and decide on the allocation of resources of health services and are responsible for the overall planning and finance of these services in the respective county. The councils generally follow the vaccine progammes recommended by the NBHW. The brand of vaccine to use is decided by a regional pharmaceuticals committee, often in collaboration with a group of vaccine experts. When this decision has been taken, an agreement is made with the vaccine producer directly or through Apoteket AB (National Corporation of Swedish Pharmacies) and a settlement of purchase for the whole county or for a larger region is made.

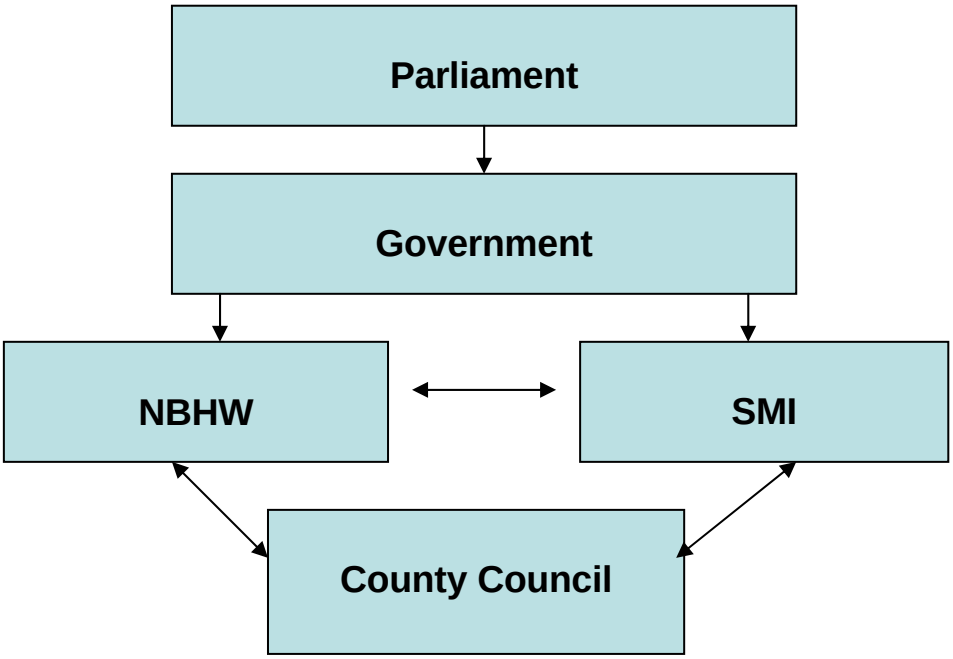

Figure 1. Graphic presentation of Swedish health-care participants.

RECOMMENDED VACCINATION PROGRAMME

Since 1980 the NBHW has been responsible for recommending the principles of the general childhood vaccination program. There are no mandatory vaccinations in Sweden, and the parents thus make the final decision to accept the offered vaccination or not. If a parent should want to vaccinate their child with other vaccines than those included in the national recommendations or with another type of vaccine than those purchased by the county/municipality this will have to be done at the parent's own expense at a vaccination clinic. The vaccines included in the national childhood vaccination program, see Table 1, is offered free of charge to all children living in Sweden.

Table 1. Vaccine programme according the recommendations from the National Board of Health and Welfare, ordinance, 1996:1 and 2005:18

	General section					**Selective section**		
Age	Diphteria, D Tetanus, T Pertussis, P	Polio	Hib	Measles Mumps Rubella	Responsible for vaccination	Tuberculosis	Hepatitis B	Responsible for vaccination
Newborn						Children at higher risk		Practicing doctors
3 months	I	I	I		Paediatric health-care			
5 months	II	II	II					
12 months	III	III	III					
18 months				I				
5–6 years		IV						
10 years	IV				School health-care			
12 years	II							

Children at high risk of hepatitis B in the selective section in Table 1, refer mainly to infants to mothers that are HBsAg positive and in order to prevent transmission vaccination is offered to the child soon after birth.

The NBHW recommendations in papers I-III

Influenza vaccination: The NBHW recommends influenza vaccination for all persons with coronary and/or pulmonary disease, and for persons 65 years of age or older (ordinance SOSF 1997:21).
MMR vaccination: In 1982, the combined vaccination with measles, mumps and rubella, MMR, was introduced as a two-dose regime in the Swedish childhood vaccination programme. The first dose is recommended to be administered when the child is 18 months of age at the child health-care centre, CHC and the second dose at 12 years administered by school health centres, SHC (ordinance SOSF 1996:1).
Hepatitis B: NBHW recommends hepatitis B vaccine for a number of groups at higher risk of exposure, among them health-care workers (HCWs) with frequent blood contact.[25] The employer is responsible to decide who should be regarded to be at risk and who should therefore be offered the vaccine.

SWEDISH SURVEILLANCE

Disease surveillance

In Sweden the national communicable disease surveillance system is based on statutory case reporting of 58 selected diagnoses, specified and regulated through the SML. Accordingly, all identified cases of measles, mumps, rubella and hepatitis B are reported to this system both by laboratory and clinicians.

Case reporting is done with full identification to the County Department for Communicable Disease Control (SME) where the patient is residing, as well as to the SMI. Notifications are made in parallel both by the physician examining the patient, and by the laboratory that identified the agent. Reports from these two sources are merged in the national computerized surveillance database, "SmiNet" at SMI, using the 10-digit personal identification number to prevent duplicate case reports. Data are also manually checked for errors on a regular basis. A recent study of the proportion of locally diagnosed cases reported to the National Communicable Disease System, NCDS, demonstrated that the system benefited from parallel reporting, with an overall sensitivity for all diseases combined of clinical and laboratory notifications of 91.6% and 95.9% respectively. The sensitivity for both clinical and laboratory notifications were markedly higher when using the national electronic reporting system, SmiNet.[26]

Influenza

Influenza is not a reportable disease, but the epidemiology of influenza in Sweden is assessed through an influenza sentinel reporting system. There are 96 sentinel units spread out over the country recruited by the SMEs. Both individual general practitioners, GPs, and larger health care centers participate in the system and reports were received from 20 out of 21 counties during 2005. The report consists of number of patients seen with influenza-like symptoms, date of visit, age and sex, and these data are sent weekly to the SME and forwarded to the National Influenza Centre at SMI.[27]

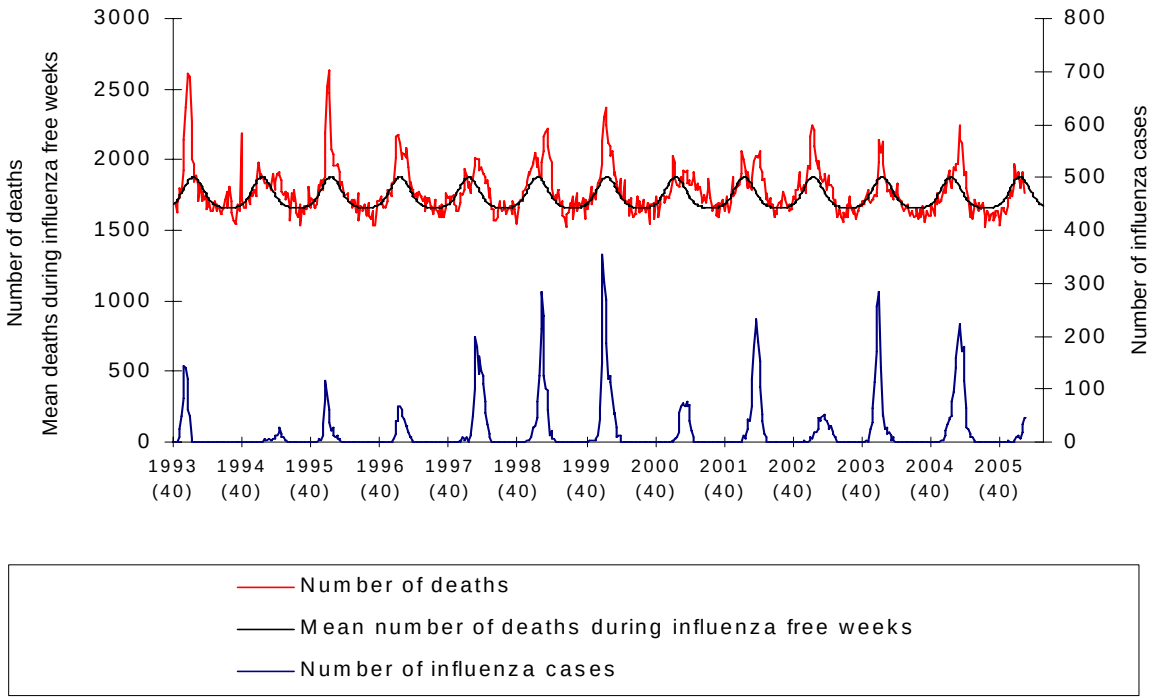

Figure 2. A way of assessing the burden of influenza is to estimate the excess mortality during influenza seasons.[28] Reports of laboratory-verified influenza diagnoses are received from 24 laboratories from all over the country to SMI. At the end of each influenza season information from Statistics Sweden, SCB, on weekly death rate in Sweden is gathered. The mean weekly death rate for influenza-free weeks between

week 40, year 1993 and week 20, 2005 has been calculated by the National Influenza Centre at SMI, and used as reference for the demonstration of weekly excess mortality along with the number of laboratory-verified influenza cases during the same period.[27]

Hepatitis B

The reported incidence to the NCDS of hepatitis B serology positive persons was 3.4 / 100 000 for 2005 (domestic cases only). At intervals, there are outbreaks of hepatitis B in subgroups such as intravenous drug users; this was seen in 2002 and 2003 increasing the incidence of domestic cases to 4.0 and 4.7, respectively. Including immigrants and others who have acquired their infection abroad, annual incidence amounts to between 15 and 20 during the last five years. The number of cases of occupationally acquired hepatitis B recorded since 1985 is displayed in table 2 (Statistics on reported communicable diseases in Sweden are available at: www.smittskyddsinstitutet.se)

Table 2. Number of confirmed cases of occupationally acquired hepatitis B by occupational category reported 1985 – 2004, source of information SMI.

Occupationally acquired hepatitis B infection among Swedish health-care professionals

Occupational group	1985-1990	1991-1995	1996-2000	2001-2004
Physician	5	1	0	0
Nurse	6	2	1	0
Assistant nurse	3	1	0	0
Laboratory staff	0	1	0	0
Dentist	3	1	0	0
Dental nurse	1	1	0	0
Total	**18**	**7**	**1**	**0**

SURVEILLANCE OF VACCINE COVERAGE

Childhood vaccination program

The "gold standard" to assess the overall effectiveness of a large-scale vaccination programme is by observing a decrease in the incidence of the disease. Figure 3, shows the effect on morbidity in measles of the implementation of vaccination against measles in 1971 and later on the combined vaccine for measles, mumps and rubella, MMR. The introduction of measles vaccine in 1971 only reached levels from 46 up to 63% coverage in the birth cohorts of 1974 to 1978 (according to statistics gathered in 1981). The low coverage was commented to be due to doubt about vaccine efficacy both among health-care professionals and the general public. When the vaccine was replaced by the combination vaccine MMR in 1982, coverage rose to over 90% within two years. The implementation of the vaccine has successfully diminished the burden of disease to a few or no cases of measles in Sweden per year.

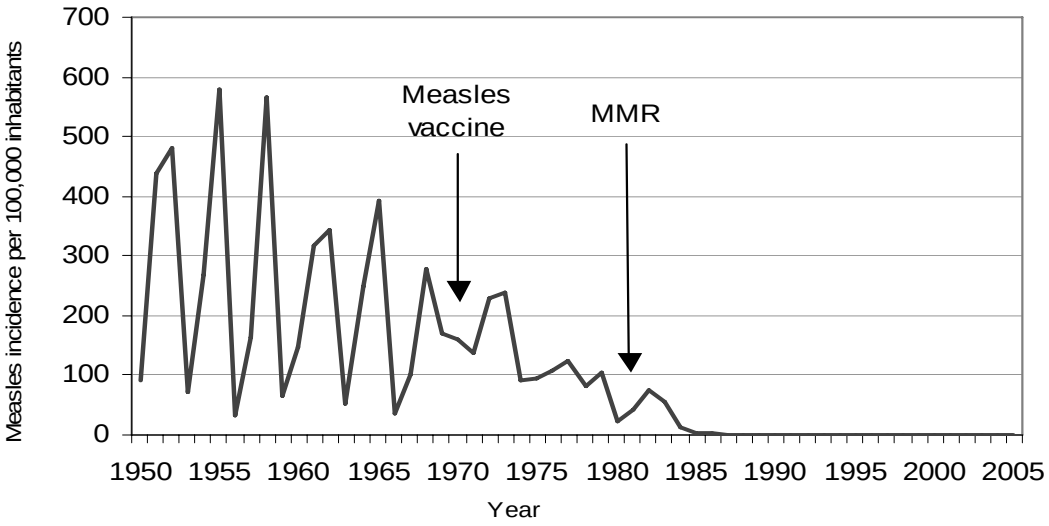

Figure 3. Measles incidence per 100.000 inhabitants in Sweden, 1950 – 2005. Data on number of measles cases attained from Malin Arneborn, SMI and populations statistics retrieved from SCB.

The vast majority, 98-99%, of all children in Sweden are registered and receive their vaccinations at a Child Health Centre (CHC). A reporting system to assess vaccination statistics from the CHCs was introduced in 1981. This systematic surveillance is performed in collaboration with the County Consultant in Child Health-Care and the Department for Epidemiology at SMI. Data for these reports are gathered by the nurses at the CHCs in January each year. Data collected are:

- number of children registered at the CHC on the 31st of December who the previous year reached the age of two
- number of these 2-year-olds vaccinated with the general recommended vaccinations
- number of the 2-year-olds vaccinated with the selective vaccinations against hepatitis B and tuberculosis (mainly children to immigrants)

Of the 21 counties in Sweden, 19 are reporting their data by form to SMI. Two counties have a different registration system based on an individual level and their data may sometimes be incomplete for some of the early vaccinations. Their data for MMR vaccine is however considered valid and therefore included when calculating national coverage for MMR (personal communication Victoria Romanus, SMI).

In the annual national report from SMI, coverage for MMR at two years of age reached 90% two years after the introduction in 1982. The maximum coverage was 96.8% in 1996, but during the following years coverage showed a slow decline until 2001 when it sharply fell to 88.4%. Since then, there has again been an increase, and in the report for 2005 overall coverage was 94.5% for MMR.[29]

Influenza vaccine

There is to date no national registration of coverage for influenza vaccine. At county level attempts have been made during recent years to improve information on number of vaccinated person age 65 years and older. In some counties computerized systems

have been constructed to facilitate surveillance.[30] In other counties, questionnaires are used to assess coverage,[31, 32] and in some the pharmacy registers of number of vaccine doses distributed give an estimate of the vaccination activity. Data collected by these different methods gave an estimated national coverage in the age groups over 65 of just over 50% in the autumn of 2004.[33]

Hepatitis B

To date there is no national or regional registration system available for assessing number of persons vaccinated with hepatitis B beyond the administered vaccinations through the childhood vaccinations registration. Employers do not maintain any registry of staff who have accepted and received hepatitis B vaccine due to occupational exposure.

Future developments

Apart from the data from SMI on coverage among two-year-olds in Sweden, there is currently no national register of vaccinations performed where coverage data can be retrieved. On a regional basis there are some register systems developed, for example in the county of Småland.[30] However, a computerized national vaccination register, Svevac, is under development with a primary objective to monitor vaccine safety.[34] This system is planned to be taken into active use for registration of childhood vaccinations in the near future and it has already been pilot tested in several CHCs in the country. When fully developed the intention is that all vaccinations an individual receives should be registered in this system.[35, 36]

Cost for influenza vaccinations

During the investigated years in paper I the cost for the individual for a dose of influenza vaccine in the county of Östergötland was 160 SEK (approx. 18 euros). For persons belonging to the groups listed in the national recommendations this cost was included in the "high-cost-limit". Under this scheme, a patient pays the entire cost of prescribed pharmaceutical preparations up to SEK 900. Above this a rising scale of subsidy comes in, with a high-cost-limit, meaning that the patient never has to pay more than SEK 1,800 in any twelve-month period.

There is a large variation of the cost for influenza vaccine between the counties in Sweden ranging from180 to 0 SEK for the individual. The situation in the spring of 2006 is that 12 of the 21 counties offer the vaccine free of charge for those included in the national recommendations, the county council of Östergötland adapted the cost-free offering in 2005.

HEPATITIS B VACCINE - WHO RECOMMENDATION

The WHO, recommends that all member countries to include vaccination with hepatitis B vaccine in the general recommended vaccination programme.[37] The Scandinavian countries have so fare chosen not to, mainly due to low prevalence of the disease.[38] Recommendation are instead focused on known risk groups such as intravenous drug users, HCWs with frequent blood exposure, and to children born to mothers who are HBsAg positive. When a child is found infected, close relatives and class-mates at the day-care centre should also be offered vaccination.

New vaccines

Before a vaccine against a disease is included in a national vaccination programme a series of considerations is taken in account - pros and cons are weighed against each other in a long-term perspective. The National Public Health Institute, KTL, in Finland uses the following model of questioning around every proposed change in the national vaccination programme:[39]

- Will a general vaccination improve public health? If yes, move on to the next question.
- Is the vaccine safe for the individual? If yes, move on.
- Is it possible that general vaccination could result in any unfavorable effects that outbalance the benefits? If no, move on.
- Is there a reasonable balance between cost and benefit?

In Denmark, Statens Serum Institute, SSI, uses a health technology assessment strategy:

- Epidemiology “Do we have a problem?”
- Technology “Can a vaccine solve the problem?”
- Attitudes “Do we (parents) want this solution?”
- Organization “Can we manage it?”
- Economy “Can we afford it?”

When vaccine against Haemophilus influenzae typ B was introduced in Sweden in 1992-93, Garpenholt and colleagues studied factors of importance for implementation.[40] The topic was further addressed in Garpenholts thesis where the following factors where discussed:[41]

- The vaccine product: production, distribution, efficacy and safety etc.
- Conception of disease: disease presentation.
- Government, economy: economy analysis, financing.
- Public decision-making: government argumentation, individual choice, and public opinion.

One of the important aspects to consider is attitudes and acceptance of a new or changed strategy regarding immunization. Assessing knowledge and attitudes towards any new recommendations is therefore of great importance.

STUDY SITES

In study I - III the county of Östergötland was the site of study. The population of Östergötland is just over 415 000 inhabitants which accounts for around 5% of Sweden's total population. This county is sometimes referred to as a good average of Sweden in socio-economic and demographic terms. Data for comparison on variables of interest for paper I and II are shown in table 3 and 4 for the county and for Sweden as a whole.

Table 3. Comparison of the County of Östergötland and Sweden (factors of interest in Study I.).

	Östergötland	**Sweden**
Proportion of inhabitants age 65 years or older	17.6%	17.2%
Average life expectancy, women 2000 – 2004	82 years	82 years
Average life expectancy, men 2000 – 2004	78 years	78 years
Proportion if inhabitants ≥ 65 years of age who live in "service homes"	7.8%	7.2%
Proportion of all reported deaths among ≥65	5.3%	5.3%

Table 4. Comparison of the County of Östergötland and Sweden (factors of interest in Study II).

	Östergötland	**Sweden**
Proportion of children age 0 – 6 years	7.1%	7.4%
Mean age of the mother at the time of the firstborn	28 years	29 years
Mean age of the father at the time of the firstborn	31 years	31 years
Level of education among persons 20 - 49 years of age: Compulsory school	12%	12%
High school graduate	51%	51%
>High school graduate	33%	34%
Proportion of persons employed aged 16– 64	59%	61%

Figure 4. Map of Sweden with the 21 counties. The study area in Study I – III, the County of Östergötland is marked with gray.

In study IV the sample was drawn from the national level.

AIMS

To assess coverage and reasons for non-vaccination for some of the most important vaccinations presently recommended by the National Board of Health and Welfare

- influenza vaccine for the elderly
- MMR vaccine for children
- hepatitis B vaccine for health-care staff,

and to assess parental knowledge of hepatitis B, and their attitudes towards hepatitis B vaccination for their children.

METHODS

In all four studies included in this thesis the investigated sample of subjects have been collected from a defined and identified population.

In study I the sample of subjects to be interviewed was drawn from a group in which coverage with influenza vaccine should be high, namely those who had moved from their homes to special apartments within the community that gives special care for the elderly. The sampling was performed by retrieving a list from the local authority of all the available special apartments in the municipality and from this list selecting every fourth apartment. The tenant of these apartments was then called upon for an interview.

In study II the English term Well Baby Clinic, WBC was used for the Swedish institution "barnavårdscentral", BVC. A more common translation for this facility is Child Health Centre, CHC, and henceforth the term CHC will be used in this thesis.

In study II CHCs with a reported coverage for MMR in 2001 of 90% or lower were selected for investigation. This applied to 17 of the 40 CHCs in the county. Data on each child born 1998, 1999, and 2000, who were registered at 12 of the 17 CHCs was collected. Data consisted of: date of birth, personal identifying number and if and when MMR vaccination had been administered.

In the third study HCWs with frequent blood exposure was the population of interest. The survey was therefore concentrated to staff working at departments and wards where blood exposure could be presumed to be frequent. The entire staff working in a number of such departments at the Linköping University Hospital during a 24-hour period was selected as the study base.

In the fourth study parents to children born in 2002 were sampled from a national registry. The child born in 2002 was at the time of investigation (October 2005) older than two years of age and should recently have received all the recommended vaccinations in the childhood vaccination program. The next vaccination in the schedule is the polio vaccine at the age of 5-6 years.

Paper	Vaccine	Study period	Study population	Methods
I	Influenza	May to July 1998-2000	people 65y or older living in “service homes”	Face-to-face interviews using a questionnaire
II	MMR	January/ February 2003	All children born 1998, 1999, and 2000 registered at 12 included CHCs	Register data from CHC files
III	Hep B	May/June 2004	HCWs working in 6 highly specialized dept at a University Hospital	24 hour prevalence survey with a paper questionnaire
IV	Hep B	October/ December 2005	Parents to children born 2002	Paper versus web questionnaire

DATA PROCESSING

In studies I, III and IV all or, in study IV, some of data has been supplied by written questionnaires. In one case, study II, data consisted of paper registry lists. All written data has been transferred into computerized statistics programs. When entry was completed, list of data has been created to facilitate control for any data entry mistakes. If any data was missing or needed to be clarified, efforts were made to complete these when possible by contacting the interviewee once again. When missing information was of demographic nature and these data were available by for example information from the national population register, data were completed. No completion of data was entered before thorough confirmation and double-checking.

STATISTICAL TOOLS

EpiInfo 6.0.2 was used in papers I and III, and JMP 4.0.2 were used in papers III – IV. Differences in proportion in papers I and III was tested by chi-squared and a level of $P \leq 0.05$ was considered significant. In paper IV differences in proportion was tested by logistic regression, and a level of $P \leq 0.05$ accepted as significant. EpiInfo 2002 and SAS were the statistical tools in paper II, and logrank test was used to test for differences in coverage between cohorts.

MAIN RESULTS

STUDY I

A total of 599 persons with a mean age of 83 years were interviewed over the three periods investigated. Vaccine coverage increased over the years from 25% up to 31% in the year 2000.

All subjects were asked if they were taking any prescribed medication. If there were any drugs against cardiac or pulmonary disease, the subject was classified as suffering from such disease. Using this way of defining cardiac and/or pulmonary disease 56% of the 599 interviewees were categorized as having these conditions.

Figure 5, shows vaccination status and pre-existing illness: proportion of subjects vaccinated against influenza by gender and by pre-existing cardiac and/or pulmonary disease.

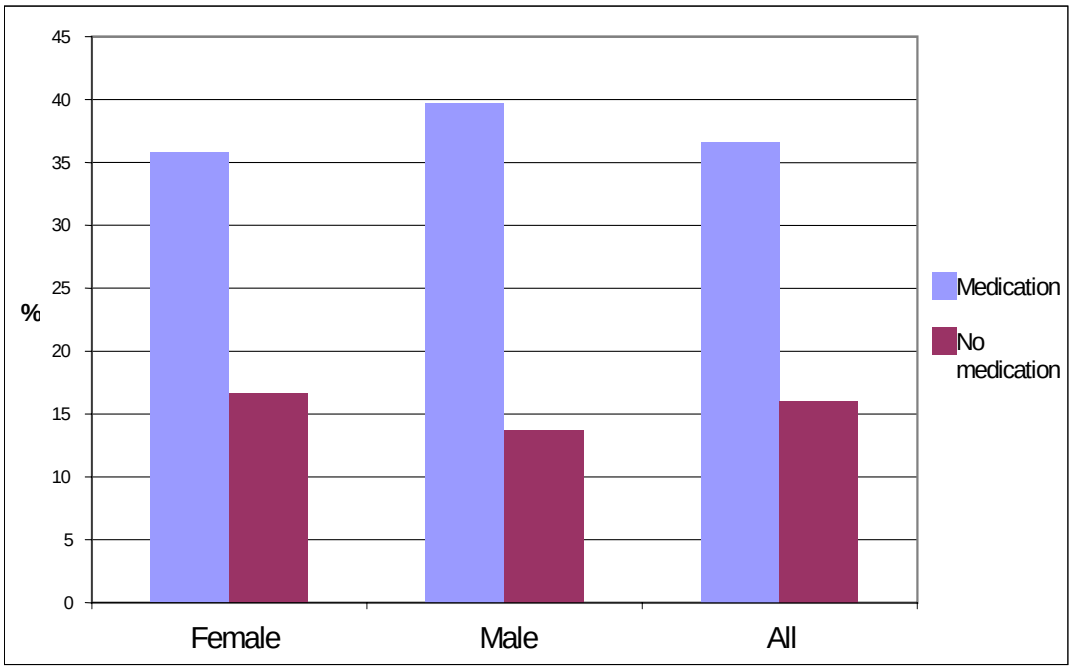

Figure 5. Percentage vaccinated among those taking prescribed medication for cardiac/pulmonary disease verses those with no medication

When analyzing the change in coverage over the three years it was found that the group on cardiac/pulmonary drugs accounted for the whole increase seen (25-30%). In the "un-medicated" group coverage was consistently low around 16%. Having knowledge of the national recommendation for influenza was a significant ($p<0.005$) factor for the probability of being vaccinated.

The subgroup of 264 subjects that had not received the vaccination was asked the question: Why were you not vaccinated? The replies were grouped and labeled in 7 categories. The pre-dominant category for overall answers was “No need”. The most common reply in this category was: “I’m too old for that” and “Vaccinations are for children”. On five occasions the cost of the vaccine was given as reason for non-vaccination.

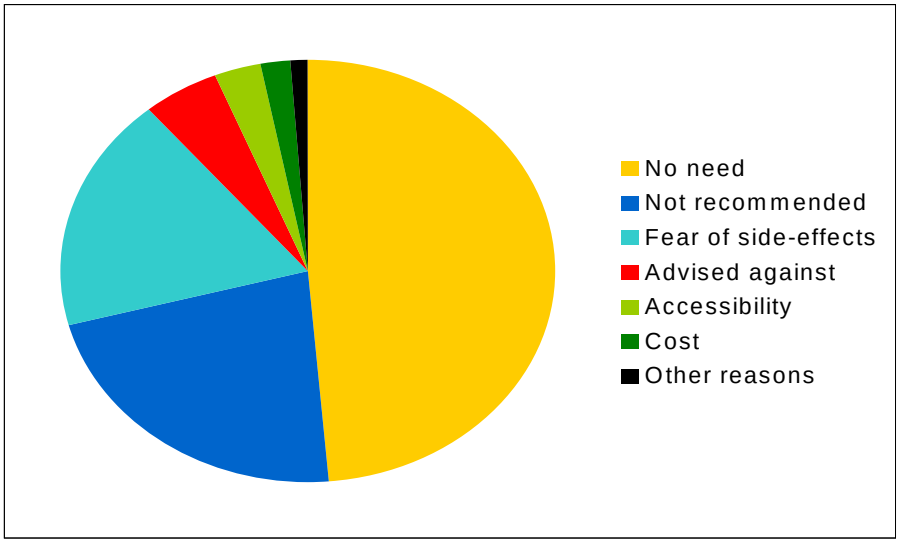

Figure 6. Reasons for non-vaccination given by 264 un-vaccinated subjects, in order of importance.

STUDY II

Information of vaccination status for MMR was attained for a total of 3 871 children, of whom 285 (7%) had no date of vaccination registered in the CHC files. Number of children vaccinated and age when this was done in the three age cohorts, born 1998, 1999 and 2000, are shown in Figure 7.

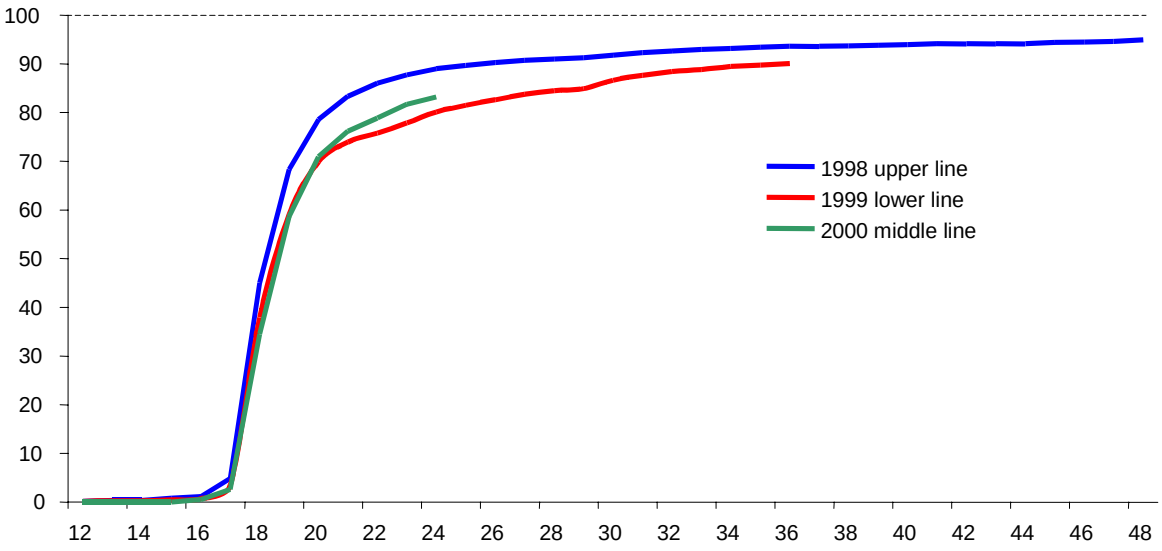

Figure 7. Vaccination coverage (%), according to the files at 12 child health centres by month of age in the three cohorts of children born in 1998, 1999 and 2000.

The Kaplan-Meier curves show the proportion vaccinated in each cohort as a function of age. The difference between 1998 and 1999 is highly significant, as also between 1998 and 2000 although an increase of coverage can be seen in the 2000 curve. The curve for the 1998 year cohort indicates that some 4-5% of the children will remain unvaccinated.

Table 5. Number and percent of children vaccinated in the three age cohorts. The figures for 24, 36, and 48 months are from the present study, the column for national survey gives reported coverage for the 12 CHCs of the study in the annual national survey, which assesses coverage in children 24-35 months old.

Year of birth	Sample* n	Sample Vacc % 24 mo %	*National Survey "24" mo %*	Sample Vacc % 36 mo %	Sample Vacc % 48 mo %
1998	1316	88.9	*93.4*	93.6	94.9
1999	1262	80.2	*85.2*	90.1	--
2000	1293	83.2	*91.0*	--	--

*12 child health centres of the total 40 CHCs in Östergötland

The national surveillance system for childhood vaccine coverage collects data on children who are 24 to 35 months old. The average age for the children in the national coverage is thus some 30 months of age. When comparing the national data with data from this study for the cohort of children born 2000 the national surveillance system reports coverage of 91% compared to the study data at 24 months of 83.2%. There is thus an increase of vaccination beyond the actual age of 24 months up to an average of 30 months old of some 7.8 percentage units.

The 285 subjects with no date for MMR vaccination were further investigated using telephone interviews.[14] In this study (not included in this thesis) of the original 285 subjects 203 were contacted. Of these 203 parents one declined to participate, and three interviews were excluded due to language barriers. A total of 199 telephone interviews were analyzed corresponding to 70% of the original 285 subjects. Mean age of the children at the time of the interview was 43 months, ranging from 27 to 64 months. Thirteen percent (26/199) reported that their child had received MMR vaccine, and that this was done prior to the collection of our data, but not registered in the CHC file. The remaining 173 interviews were further analyzed.

Sixty percent (103) of the parents had decided to postpone the MMR vaccination for their child and 40% (70) had decided to abstain. The most common reason given overall for not having their child vaccinated at the stipulated age of 18 months was fear of side-effects. This reason was significantly more pronounced among those who abstained, and this was also true for the factor "better with natural immunity".

Figure 8, shows the five most common sources of information on MMR. Media was most frequently mentioned (82%) followed by the CHC (29%). Comparing the responses by order of decision to postpone or abstain a difference is seen. The postponement group more frequently mentioned the CHC as a source, 35% compared

to 20%, and the abstention group referred to anthroposophist in 31% compared to 3%. To questions as to whether they had discussed their decision with the CHC staff, 49% of the postponement group said that they had this opportunity versus 66% of the parents who chose to abstain (95% CI – 31.7 to 22).

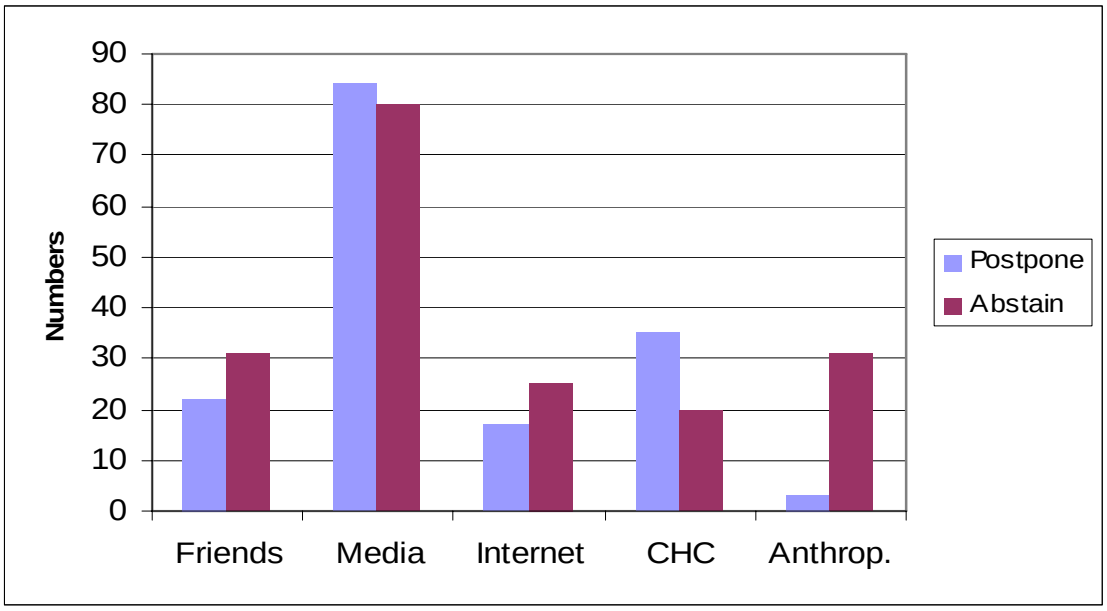

Figure 8. Sources of information on MMR vaccination. (More than one source could be reported by an interviewee).

STUDY III

Of the 369 analyzed questionnaires on vaccination status for hepatitis B vaccine, 147 (39.8%) of the HCWs reported to be fully vaccinated, 146 (39.6%) were partly vaccinated and 76 (20.6%) had not received any hepatitis B vaccination at all. The subjects' vaccination status when sorted in different age categories is shown in Figure 9.

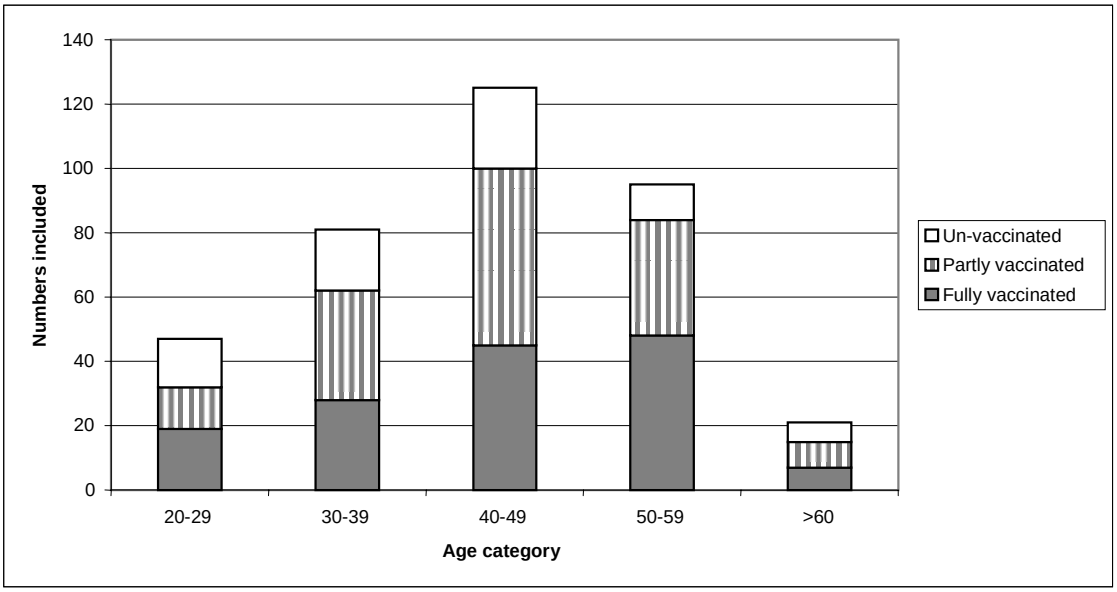

Figure 9. Number of subjects in each age category, and number fully, partly, and not vaccinated.

The largest proportion of fully vaccinated (58%) HCWs were aged 50-59 years, the largest proportion of unvaccinated (32%) HCWs were aged 20-29 years. Of the non-vaccinated 72/76 (95%) claimed that they would accept the vaccine if offered and of the 146 partly vaccinated the most common reason for not completing the vaccination schedule was that it had been forgotten 62 (42.5%).

The participants were asked a question on how often they perceived to be at risk for blood-borne disease at work. They were given six different alternatives varying from once a day, once a week, - up to once a year, or never. The responses were later group in two groups; once a week or more often, and once a month or less often. When the vaccinated group was compared with the un-vaccinated it was found that those in the vaccinated group significantly more frequently (p= 0.02) felt fear once a week or more often than the un-vaccinated group.

STUDY IV

Parents' knowledge of hepatitis B and their attitude towards hepatitis B vaccination for their child if offered was surveyed by questionnaires either by a paper or web version. Number of replies by the way of response paper or web is shown in Figure 10.

A total of 1229 out of 1992 (62%) questionnaires were completed. The final overall response rate for the paper questionnaire was 55% (996/1817), and 15% (233/1507) for the web version. The majority of web responses were received within 7 days of the distribution of both the first information and the reminder: 79% (142/179) and 74% (40/54) respectively.

The respondent was in 1141 cases the mother of the child and in 88 cases the father. There was no difference by way of responding related to the parent's gender. There were some missing demographic data in 38 of the paper questionnaires, these were completed by the investigator with information from the national population register. There were no missing data in the web replies.

Knowledge of hepatitis B was high overall, 90% reported to be aware of this disease. The knowledge was to a significantly higher (p= >0.001) among parents with education beyond high school. The only difference seen between those who responded to paper versus web questionnaires where that parents with higher level of education had a higher tendency to respond by the web (p= 0.001).

Factors that affected a positive response to the question "would you have your child vaccinated with hepatitis B if offered?" was having their child fully vaccinated according to the national recommendations (p= 0.001) and responding to the web questionnaire (p= 0.006).

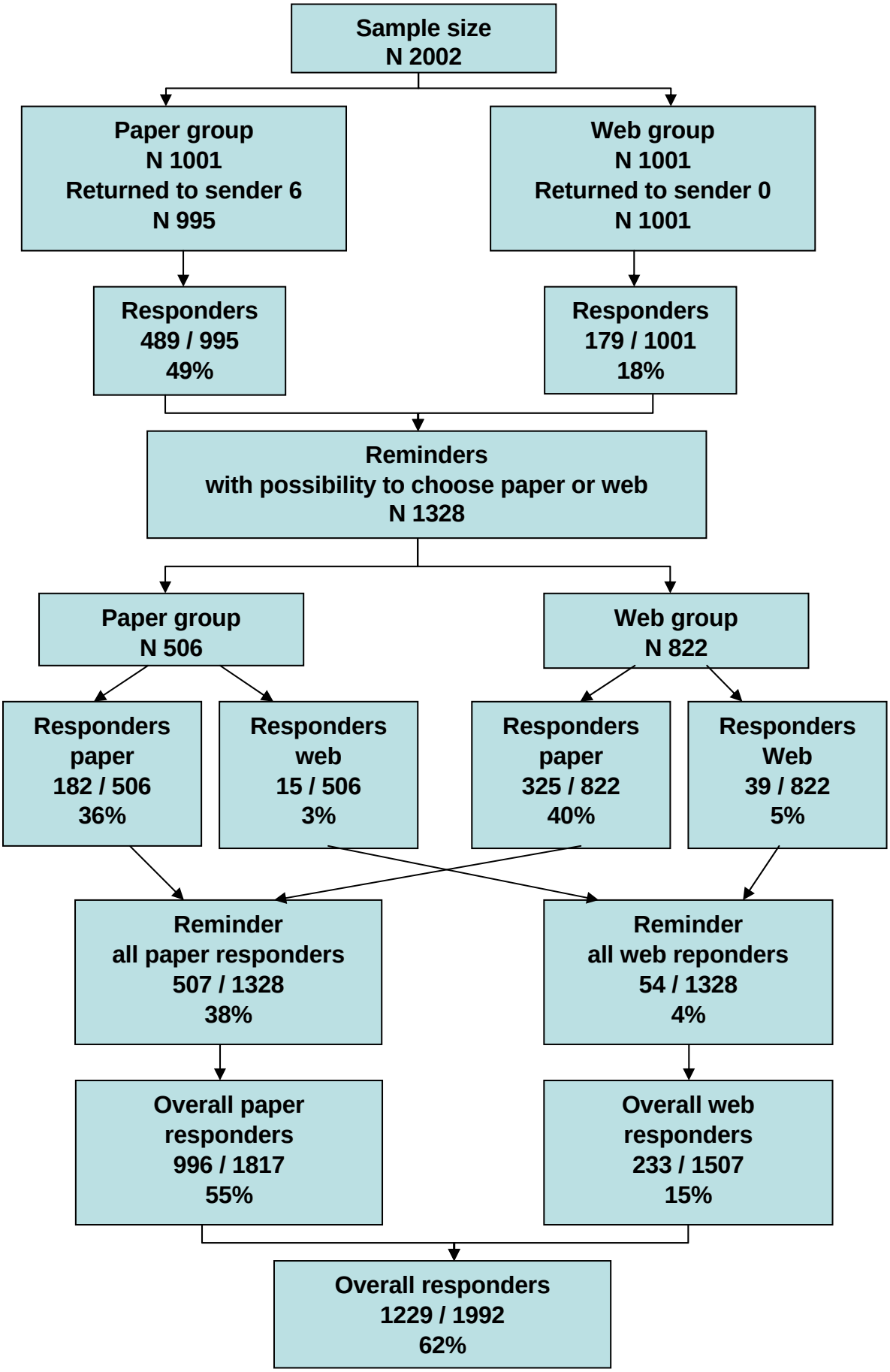

Figure 10. Summary of the response rate for the survey.

ETHICAL CONSIDERATIONS

In study I, III, and IV participation was voluntary. Detailed information on the different studies were given:

- Direct to the person when called upon, study I. The investigation was performed during influenza free periods in each of the investigated years. This to avoid influencing the interviewee or mistakenly being perceived as promoting vaccination, not only collecting data. Theoretically, an ethical problem could arise if the questions created concerns or anxiety among those not vaccinated that they had missed out on this. However, since the interviews were done in the summer, there was every chance to get the vaccine the following autumn.

- In study II registry data from the files at child health centers was retrieved. For this part there were no ethical considerations to be regarded.

- In study III, HCWs were informed about the 24-hour survey, and written information was attached to all questionnaires. We could not foresee any major ethical problem with the survey.

- In studies IV information was sent by mail along with a paper questionnaire and/or a personal password and login to a website. The parents had the choice to answer the questionnaire or not. Theoretically, we could have raised some concern in the parents of hepatitis B as yet a new threat to their child, but we did not get any such reactions.

Approval from the regional ethics committees in Linköping was received for studies I – III, and for study IV the regional ethics committee, Karolinska Institute in Stockholm approved the survey.

DISCUSSION

Vaccines are among the most effective public health interventions used today, as is illustrated by the fact that all countries of the world have vaccinations programmes for their populations. These are mainly aimed at protecting children against the common childhood diseases but other population groups and other vaccines are also receiving increasing focus. In spite of the success of many of these programmes in saving millions of lives every year, implementing the programmes on a population level still entails many problems. Assessing the efficiency of the implementation and analysing factors that are obstacles to achieving high coverage is therefore a crucial part of the work of public health authorities.

One of the main threats to well-functioning programmes with high coverage has been to keep the trust of parents in the need and safety of vaccinations. A recent example of distrust in a vaccine was a study suggesting a possible link between autistic spectrum disorders in 12 children and MMR vaccine presented by a research group.[42] This article was published in 1998 and received wide-spread media coverage.[43] The effects of these allegations were seen in MMR vaccine coverage in many western European countries: in the UK coverage declined from 91% in 1997,[44] to 82% in 2004.[45] Also in Sweden, a sharp decline was noted in 2001 when coverage had fallen from almost 97% in 1996 to 88.4%.[46] This happened despite a large number of studies that refuted any connection between MMR and autism.[47-50] These studies did not generate the same media coverage as the original article, instead it has been up to health-care providers to distribute this knowledge and to refute misconceptions among parents. This example makes it clear that the understanding of the reasons for non-vaccination and addressing these in communications with parents is crucial in the work to keep high coverage of vaccinations – especially when vaccination has been so successful as to make the diseases almost disappear, no longer posing any tangible threat.

COVERAGE

One of the objectives of this thesis was to assess coverage for three of the NBHW recommended vaccinations in different populations. These where MMR in pre-school children, influenza in the over 65 and hepatitis B among health-workers at risk for blood exposure. The best data can be found for the general childhood vaccinations. Almost all children (98-99%) in Sweden receive their immunizations through the CHCs, and the reporting from these about these immunizations is well established and has for more than 20 years provided valuable information on coverage and changes over time. The achieved coverage for the offered vaccines have all reached high satisfactory levels.[29]

When estimating coverage in children it is important not only to know that the child has been vaccinated but also at what age. On an individual level the goal is to protect the child as early as possible while at the population level it is to vaccinate as many as possible to achieve a herd immunity and thereby protect children that are not yet vaccinated. A good vaccine coverage reporting system takes both these aspects into account, which usually means that the dates of vaccinations at an individual level are

needed. However our study of register data revealed that the available statistics is not reflecting the coverage for children at the age of two. The way the data is collected reflects coverage for children who are between 24 and 35 months of age. The current surveillance system thus overestimates coverage at the age of 2 years by close to 5%, but at the same time underestimates final coverage by a similar figure by not recording vaccinations taking place after 35 months of age. It could be concluded that this system does not give any information on an individual level, it is thus not possible to retrieve data on timeliness of vaccination. It also does not give complete data on all children receiving a vaccine which makes the estimate of herd immunity unreliable. This illustrates that even a very efficient reporting system sometimes needs to be complemented by focused studies to evaluate the validity of data presented. The need to achieve timeliness of vaccination and possibility for surveillance of this aspect is recognized in several studies.[13, 51, 52]

Attaining figures on coverage for influenza and hepatitis B among adults is much more difficult in Sweden. There is no national system for systematic registration or reporting of adult vaccinations. Administered vaccines are registered on the personal vaccination card or in the patient file. There is thus seldom any exact figure on regional or local coverage available, and the situation is the same or worse when it comes to coverage on hepatitis B for HCWs. The effect of this lack of a national system has been that local and regional public health officials have developed their own systems and that there is often a local and regional knowledge of how the programmes work but it has been difficult to compare the success of programmes in different regions and in an efficient way analyze the effect of new interventions.

One example of this, is that since the coverage data for influenza collected in this study was gathered in 1998 – 2000, efforts to increase the number of immunized people aged 65 years or older have been made all over the country. However a difficulty when trying to compare the effect of these interventions in the different counties is that a variety of methods were used to assess coverage for influenza. Information collected for coverage during the influenza season 2005 –2006 from different counties consisted of data:

- on individual basis in one case
- from telephone surveys
- from invoices for the cost of the vaccine
- on number of distributed doses vaccines
- and from paper questionnaires (the most commonly used method)

Not only the methods but also the validity in the collected data varies widely, but as long as the level of coverage has not reached levels where smaller changes can be of interest this is of less importance. When there is no comprehensive national system there could be a role for a method like the one used in our study. This is a method that is relatively easy to use and can be carried out by student or health–care staff in a timely fashion and give a reasonably accurate figure that can be compared between different geographical areas.

In a recently presented study by Kroneman et al., coverage for influenza vaccine among high-risk persons was investigated in four European countries: Germany, Spain, Poland and Sweden. Using a close-ended questionnaire a telephone survey was carried out as a part of a national telephone-omnibus with a randomly selected of respondents. Coverage for influenza among the elderly (65+) interviewees was 53% in Germany, 18% in Poland, 67% in Spain, and in Sweden a coverage of 46% was found; these data were collected in March and April, 2004.[53] Almost at the same time, the Swedish Society of Communicable Disease Prevention and Control presented their data on estimated influenza vaccine coverage in Sweden that had been collected during the same time period. Using the various methods described above, a coverage of 52% was found in the same group of people.[33] This shows that in spite of all the theoretical limitations a reasonable estimate of coverage was achieved.

Keeping data on coverage among health-care staff has been considered as mainly being the responsibility of the employer who has the legal responsibility to protect the employees from microbiological threats. In our study we found that employers often stop at offering the vaccine and that the division of responsibility among employers and employees needs to be clarified.

REASONS FOR NON-VACCINATION

Another main objective of the study was to find and analyse reasons for non-vaccination for different vaccines and in different populations. In well-established childhood vaccination programmes who experience a fall in coverage this is an often discussed factor that needs to be identified and strategies developed to counteract. In our study we found that the most common reason given for not having their child vaccinated at the stipulated age of 18 months was fear of side-effects. Although this reason was significantly more pronounced among those parents who chose to totally abstain from vaccinating their child with MMR compared to those who only postponed it, parents who abstained also more commonly believed that it is 'better with natural immunity' than those who postponed. 'Postponers' often wanted the child to mature more before receiving MMR.

The background to the decision of the parent to vaccinate or not can obviously vary and different important aspects have been discussed in different studies. In the telephone survey[14] parents with a single child to a larger extent elected to postpone than to abstain from MMR vaccination. This could well be due to uncertainty as a new parent. This study also found the parents who decided to postpone vaccination seldom reported having had a chance to discuss their standpoint with the staff. In a study presented in 2005 Wroe and colleagues concluded that in terms of vaccine for MMR the decision not to vaccinate children was strongly influenced by the parental belief that harm resulting from immunization is less acceptable than the potential harm that might arise from not allowing the child to be immunized. This is called "omission bias," in which the idea that causing harm through action (commission) is less acceptable than the result from inaction (omission).[54] Receiving more information and having a chance to discuss the issue could have been beneficial for these parents in their decision-making according to results from other studies.[55-57]

The most common reasons for non-vaccination for influenza among the elderly in our study could be categorized as "No need" and interpreted as a lack of knowledge of the recommendations issued and the increased risk for the elderly when falling ill with influenza. This lack of knowledge of the recommendations for this vaccine is in accordance with other studies. In the U.S. the Medicare Current Beneficiary Survey measured annual vaccination rates since 1991 and since 1996 they also measured self-reported reasons for not receiving influenza vaccine. In the report from 2000-2001 the most frequent cited reason was: not knowing that influenza vaccination was needed.[58] In a Dutch survey of Kroneman et al. the main reason among the elderly for non-vaccination was "having enough resistance to the flu".[59] In a recently presented study of the same author reasons to refrain from influenza vaccine among high-risk persons in four European countries, was investigated. Replies from the elderly combined with replies from persons with other high risk factors gave three main reasons for non-vaccination in the European investigation. The ranking order was the same in all the investigated countries;

- I have sufficient resistance to flu.
- I do not qualify for influenza vaccination.
- Influenza is not a serious illness.[53]

All these reasons indicate lack of knowledge of the disease and of the recommendations for vaccination.

Lack of knowledge can also be seen among HCWs: an example from our study is that only nine of the 146 partly vaccinated HCWs had an appointment to receive the next dose of hepatitis B. Of the remaining 137 the main reason for not completing the course was that it had been forgotten. Among the unvaccinated subjects almost half had been offered the vaccination by their employer, but for various reasons it was never done. "I never got around to making the appointment and then I forgot it" was most commonly given reason for this. Doubt that vaccines are good for you and fear of needles were stated by only four HCWs as reason for non-vaccination. A computerized system that automatically produces reminders for those who have not completed their vaccination course and reminders to those who should receive an annual immunization could be a tool to be used by the health-care system and employers. This so they can ensure that the national guidelines are implemented.

THE ROLE OF HEALTH-CARE PROFESSIONALS

Perhaps the most important role for the implementation of successful vaccination coverage lies with the health professionals. When assessing coverage for influenza in this study population it was found to be low, at best reaching 30% in the final year investigated. The increase that was seen over the three periods surveyed appeared only in the group who had risk factors like cardiac and/or pulmonary disease. It was obvious that the fact that age alone should be a reason for having a yearly vaccination against influenza has not reached one of the target-group for the recommendation i.e. the health-care workers. In other words, these results indicate that the NBHW guidelines have not been received and/or embraced by health professionals. This indication was further strengthened by the second most commonly ranked reason for non-vaccination stated by the over 65s being "I was not recommended". This population should most likely have frequent contacts with the health-care system, illustrated by the mean age of

the interviewees being 83 years, and also their accommodation in a "service home", plus the fact that they almost all had prescribed medication of some sort; from all these facts one can conclude that this group of people should have repeated contacts with the health-care system.

Several studies from different countries have also noted the importance of health-care staff for a successful vaccination programme. In a study by Szucs and Müller where coverage rates for influenza vaccine in Germany, Italy, Spain, France and the UK were investigated it was concluded that health professionals have a key role in vaccination uptake. Both individuals who received vaccination and those who had never been immunized with influenza vaccine recognized the family doctor or nurses as having a major role in public vaccination behaviour.[60] In another study performed in Switzerland it was observed that patients views on the acceptability of vaccine were very positive and few reported ever having refused vaccination when recommended by a doctor.[61] The family doctor's role as the most important person to encourage people to be vaccinated against influenza has been recognised in other studies.[62-66] In an American study where the purposes was to characterize missed opportunities for adult vaccinations, such as for influenza, the conclusion was that missed opportunities to immunize occur frequently and this can be minimized by assessing and recording vaccination status at each visit. In this way the provider also conveys the message to their patients how important immunizations are for their health.[67] The importance of missed opportunities for the lack of high coverage in the elderly has been stressed in other studies.[68-71]

Communicating the national guidelines to all actors is important, but perhaps most to those within the health-care system who have the main role in recommending and carrying out these guidelines. Knowledge, attitudes and beliefs among these doctors and nurses should be investigated and their employers and the responsible national authorities should emphasize their important role as providers not only of the actual immunizations, but also as providers of information to the public about the benefits – and possible side-effects – of the vaccines used.

In our study on parents' reported reasons for avoiding MMR vaccination for their child we found that CHCs was noted as one of the most important sources of information. Furthermore, parents who chose to abstain from vaccinating their child with MMR were more likely to have had a discussion with the doctors and nurses about MMR vaccine than those who had "only" chosen to postpone.[14] The important role of health professionals as providers of information is also recognized when it comes to childhood vaccinations.[15, 57, 72]

Studies performed in New Zeeland have investigated the knowledge and educational needs about immunization of nurses and physicians who provided childhood immunizations. It was found that family doctors expressed a need for better resources to more effectively address parental fears and misconceptions.[73] Among the nurses, 90% identified parents' fears as the greatest barrier to achieve better coverage but they disagreed that knowledge among health professionals was a obstacle. However, the study displayed a lack of knowledge among the nurses, despite many of them feeling

confident about their knowledge base.[74] Results from several studies underlines the necessity for doctors and nurses who provide these vaccines to be well informed and up to date and to be able to relate findings from medical research to the individual parents and discuss different perspectives with them.[75-77] The majority of parents have a high acceptance of the recommendations and the most common questions are easy to respond to. But it is essential to meet also those parents who need to discuss and receive information beyond the more common queries. Verweij and Dawson described in their article the need to take parents concerns about vaccine safety seriously,[78] and the necessity of having well educated and up to date health professionals who are able to discuss vaccination issues in depth with concerned parents has been pointed out in many studies.[14, 79, 80]

Even among educated health professionals the need for professional guidance as concerns one's own immunizations is evident. In our point prevalence study presented in paper III we found that only 40% of HCWs were fully vaccinated against hepatitis B although all included would be at risk according to the national guidelines. Among the partly vaccinated, the most common reason given for not having completed the vaccination course was that it had been forgotten. And among the 20% non-vaccinated half had been offered the vaccine but then never come around to make the necessary appointment and almost all stated that they would accept if offered again. Willingness to update their vaccination status according to current vaccination policy was as high as 96% among HCWs in an Australian study, but only 24% of those reported being fully vaccinated.[81] Doebbeling and colleagues found similar coverage for hepatitis B vaccine among HCWs, and they further explored reasons stated for having accepted a vaccination. The highest ranking reason was "information obtained from professional sources" like a supervisor or a physician.[82] At the hospital investigated in study III, new employees at four out of six departments were offered the vaccine, however it was totally up to the employee to make the necessary appointment. In another Australian survey it was found that HCWs knowledge of vaccination requirements was poor. And even if consulting a physician to discuss immunization status did almost always result in a vaccination, few HCWs made such appointments.[83] A solution could be a routine where all new employees should have a scheduled appointment at the immunization clinic. The need for a more consistent approach to pre-exposure vaccination including the use of firm reminders has also been seen when investigating hepatitis B vaccination among HCWs, surgeons included, who had not completed the course of vaccinations required.[82, 84-86]

NEW VACCINE OFFERS

Introducing a new vaccine is a complicated and sensitive undertaking and possible future reasons for non-vaccination need to be taken into account at an early stage. To address the third objective of this study we investigated parental knowledge and acceptance of a possible new routine vaccine. In this situation not only reasons for non-vaccination but also reasons for accepting the offer needs to be studied. When analysing attitudes to a possible introduction of a new vaccine in Sweden we found that the most significant characteristic of parents who gave a positive response to the question "Would you have your child vaccinated with hepatitis B vaccine if offered?" was that their child had already received all presently recommended childhood

vaccinations. Coverage levels for the childhood vaccinations in Sweden are high; one can conclude that public support for the national vaccination programmes is strong. "Trust is essential for a successful programme and where it exists it should be protected" was statement made by Verweij and Dawson in their article on ethical principles for collective immunization programmes.[78] In an American case-control survey including over 2000 parents it was found that more than 90% of parents of both cases and control children believed that immunizations are of importance to the health of a child. For a small proportion of children, parental concerns about vaccine safety and their belief that children receive too many vaccines were associated with the failure to receive vaccines like MMR. They further showed that even parents whose children were up-to-date with their vaccinations were concerned about vaccine safety issues.[87] In a Dutch survey with the aim to determine attitudes of parents towards possible future childhood vaccinations against diseases such as influenza, tuberculosis, hepatitis B, smallpox, and SARS, it was found that determinants of a completely negative attitude were: high education of the parent, and being a health-care worker. They concluded that barriers might be overcome by improving health educations, and especially targeting HCWs and educated parents.[88]

METHODS

The web and Internet has provided new tools to gather information quickly, easily and cheaply. Our background for comparing paper and web questionnaires in our study on attitudes towards a new vaccine was data from Statistics Sweden that overall access to a computer and to the Internet is over 80% in Sweden.[89, 90] Furthermore the probability was high that all parents included would be within the age-span where this high access was measured, 16 - 64 years of age. We had thus expected that response rate over the Internet would be high, which turned out not to be the case. One finding from our study was that many of the returned paper questionnaires had coffee stains on them, and it could be speculated that for a parent with small children the weekends is the time to deal with the non-urgent mail received during the week. Also, replying to a short paper questionnaire is quickly done, whilst the procedure to log on to the Internet, access the right web-site, and enter the individual user name and password is more cumbersome. There could also be less feeling of anonymity when responding by web.

There have been a few studies addressing response rate in Internet surveys. Among Canadian anaesthesiologists in one study, the participants asked to complete a web form were half as likely to answer as the ones who received a paper form.[91] In a study of medical staff at the University of Buffalo, electronic response rate was slightly but significantly lower among residents, but the same as paper for faculty.[92] In another Canadian study, orthopaedic surgeons were significantly less prone to answer an emailed questionnaire on femoral neck surgery than to return a paper version with similar content.[93] Researchers at the University of Aberdeen in Scotland performed a rather complex study, in which they first sent a letter to 10,000 people, asking for consent to participate in a questionnaire study. One quarter agreed, and of these 761 provided an email address. This group was divided into two halves, one to receive the questionnaire by email, the other by post. Response rates in this – rather selected –

group were 64 and 82%, respectively.[94] It should be noted that in all these three studies, the investigators had a list of email addresses for the web questionnaire, something that rarely would be available in a population study.

A great advantage in any research is a rapid way to produce results. Web-based questionnaires have several advantages compared to paper questionnaires, such as improved data quality, and reduction of cost and time from initiation of a study to analysed data.[95-97] The use of web inquiries is surely a method of the future but in the meantime mixed-mode surveys may be a good alternative. There is also every reason to start considering the possibly different response biases introduced by web questionnaires: will data retrieved in this way be comparable to previous results from postal questionnaires? There should probably be a large number of studies comparing responses by the two methods undertaken in very different areas of epidemiology in order to establish some kind of "conversion table" between the results attained by the one and the other.

A relatively simple and rapid way to attain estimates of vaccination coverage can be by using a cluster sampling technique and face-to-face interviews. A modified such approach was used in paper I. However data collection for this study was performed by one person doing all the interviews, which is a slow and sub-optimal method to receive quick answers. More efficiently would be to use many interviewers, and then data could be collected and analysed within days. This could be done by instructing some 30 interviewers - for instance a class of health-care students - on the use of a structured questionnaire - and on how to do the sampling. These instructions should not take more than one day, and the study could be performed during the following days. If each student interviews 7 subjects this would generate a sample of 210, which would achieve a precision around the true proportion vaccinated of ± 5-10 percentage units. Another advantage is that the interviewers would meet each individual person, which increases the likelihood to attain data from a vulnerable population where the likelihood to retrieve a high response rates in a postal questionnaire would be slim.

Telephone interviews presents another way of direct contact approach. In the follow-up study on reasons for non-vaccination of MMR[14] following study II, the parents who had a child with no date for receiving MMR was contacted. We found the propensity to respond to this contact to be far beyond our expectations: only one of the contacted 203 interviewees declined to participate. However, an important limitation of this method is the increasing number of young individuals who only use pay card cell phones and not having any registered phone. This change will negatively influence the future use of random telephone interviews.

Paper questionnaires are probably the most commonly used method in population-based epidemiological studies. When investigating HCWs' vaccination status for hepatitis B this was a convenient method to use. Information about the survey was attached to the questionnaire, and no special consent for participation is needed, you either fill in the form or you do not. In order to positively influence response rate the questionnaire was constructed with mainly close-ended questions and it fit on a one A4 side. Our intention was that it should not take more than one minute to complete the

questionnaire, otherwise we believed that there would be a clear risk that it was never completed in the stressful environment of the speciality wards investigated. Studies on questionnaire construction have shown that the length of the questionnaire is inversely related to response rate, and that short questionnaire promote the propensity to response.[98, 99]

STUDY LIMITATIONS

Validity of data in studies such as these is always affected by so-called dropouts, i.e. the subjects who do not answer the questions put to them. A limitation of the studies in this thesis is the lack of a proper dropout analyses. However the results in our studies on influenza and hepatitis are clearly in accordance with other similar investigations: influenza,[31, 32] and hepatitis[82, 83, 100] and this validates our findings. There is still missing information on influenza vaccination among the elderly with dementia and on vaccination status for hepatitis B for 40% of the HCWs at the six investigated departments. The number of responses in our hepatitis B vaccine study could probably have been augmented by expanding the time of survey, or distributing the questionnaire to all employed by paper-mail or e-mail. However, we wanted to test a quick and simple way of attaining a point prevalence in a rather large – and heterogeneous – group of people, and we feel that we probably were not too far off the real figure. In the influenza study, more information could have been collected by researching all the patient files, but then again, this would have been much more time and resource consuming study.

In the registry investigation in paper II missing data was not a problem. Instead the limitation lies in the selection of CHCs with coverage for MMR of 90% or lower. In retrospect it would probably have been more informative to collect data from all possible CHCs in the county, since this would have given an unbiased estimate of the timeliness of vaccination among all the children registered at a CHC in the county. It would also give a possibility to compare if there were any differences between CHC with high coverage and those with low. However, our main interest was to study reasons for non-vaccination, and we thus chose the CHCs where the number of non-vaccinated children would be highest.

In the study using the paper and web questionnaires replies were received from 62% of the households. We could not find any geographical clusters (north/south, urban/rural) among the non-responders but we have no other way of knowing whether these parents differed in any way from the responders. It might have been instructive to further investigate the non-responders, for example by drawing a 10% sample from these parents and trying to conduct a telephone survey to find out if they differed in any obvious way.

VALIDITY

One of the most important problems in the interpretation of continuously collected data like surveillance data and data on vaccinations coverage concerns data validity.[101] Surveillance data might be subject to a range of factors causing bias. When it comes to vaccine surveillance missing data entry is perhaps the most common reason for bias.

One way of estimating the impact of missing data is to calculate the maximum change it could cause on the results. In the study about MMR we gathered the information of date of birth and date for receiving vaccine from the CHCs. Data on 3 781 children was collected and of these 285 had no recorded vaccination with MMR. In 26 cases parents reported that their child hade received MMR vaccine at the reporting CHC. In all 26 cases the parent stated that the child had been vaccinated prior to the time of the study. These missing entries should equal < 1% (26/3871). Considering that we had no information on 82 subjects and in a worst case scenario all of these were missing entries, the number of non-vaccinated could be in error by almost 3%, even if we have no certain indication that this should be the case. But it can be estimated that in the investigated CHCs, all of which were using paper files, missing data entry decreased reported coverage for MMR by around 1%. This may not appear very high, but in a situation where you are striving to achieve herd immunity – or even eradication – there is an important difference between, for example, 95 and 96% coverage.

Another way of dealing with missing data is to use a method that minimizes its occurrence. In the survey of parents' attitudes we also compared the use of paper and web questionnaires. We found missing data entry on 38 occasion on the paper questionnaires but none in the web version. The advantage of the construction of the web questionnaire is the reminder function. When the respondent presses the send button the application was constructed to automatically remind the respondent if there were any missing fields. In all of the cases of missing data on the postal questionnaires, data could eventually be completed with information from the national population register or the list of addresses received from the sampling. But this involved thorough confirmation and double-checking which is quite time-consuming.

Validity can also be estimated based on earlier experiences with data from the same sources collected in similar manners. In the studies on influenza and hepatitis B self-reported data on vaccination status was collected. The validity of such data especially among the elderly, can be subject to recall bias. The sensitivity and specificity of self-reported influenza and pneumococcal vaccinations among elderly persons have been investigated by several researchers.[102-104] Sensitivity for influenza was higher than for pneumococcal vaccination in studies where both vaccines were investigated.[102, 104] One explanation could be that influenza is repeated annually and therefore easier to remember. A common conclusion of these studies was that the negative predictive value, NPV, was quite high, ranging from 0.77 up to 0.94. (NPV = the true probability of not being vaccinated in a patient who reported not receiving the vaccine.) The authors concluded that based on the relatively high NPV of self-reported vaccination status of influenza and pneumococcal vaccination and also the safety record of these vaccines, health-care professionals should vaccinate a person who reports not to be vaccinated.[102-104] A case–study performed in the Netherlands were self-reported data was compared with data based on real vaccination uptake, showed that these data gave similar results.[59] In our study on hepatitis B vaccination among HCWs, we used self-reported data, and one could assume that HCWs have greater knowledge of vaccinations as well as an overall higher awareness on the subject. Thus even though

Zimmerman and MacDonalds showed that NPV was lower for a vaccine that was not repeated on a yearly basis, our findings were corroborated by other studies: schedules are seldom completed.[82, 83, 100]

There are a many different methods that can be used when investigating coverage and attitudes, and in our studies we have used several. Time frame and resources limit the choice of method. A way to minimize both these factors is to conduct surveys within a geographically convenient area. Three of the included studies were performed in one county, Östergötland, which might diminish the possibility to draw overall national conclusions from the results. However, several of our findings were in accordance with similar results from other studies. Furthermore descriptive data in Tables 3 and 4 indicate that the county of Östergötland in several aspects can be considered to be an average of Sweden. This leads us to believe that our findings are valid and can contribute to the ongoing discussions on assessment of vaccination coverage, and – more important – on reasons why everyone who should be is not vaccinated.

CONCLUSIONS

- The Swedish routine surveillance system for childhood vaccinations does not provide all the data needed to evaluate the programme, and additional, focused studies are necessary to assess exact coverage and to clarify reasons for non-vaccination.

- Surveillance systems should be developed to follow coverage for targeted vaccines, such as those for influenza and hepatitis B.

- Active refusal to vaccination only plays a minor role for not being vaccinated with the vaccines studied. The most important reasons are:
  - lack of awareness of the need to be vaccinated
  - no reminder
  - missed opportunities by health-care staff

- Health-care staff is the most important source of information about vaccines to the public. They need to be made aware of this fact, and also to be further educated.

- Systems should be designed to provide reminders for vaccines in a national programme. Responsible health-care authorities and employers should provide such reminders preferably from a computerized register.

- Before introduction of new vaccines, population knowledge and attitudes should be assessed in order to tailor any information campaign aimed at the future vaccinees (or at their parents).

- Epidemiological tools such as cluster sampling, register studies, telephone interviews, and point-prevalence studies are necessary complements to routine surveillance. However, web-based questionnaires tend to yield lower response rates than mailed paper questionnaires. Also, the possible new biases created by using web-based data collection need to be better elucidated.

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