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Severity of pertussis
Paediatric surveillance and Notification study in the Netherlands in 1997

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Abbreviations

CB	Consultatiebureau / Child Health Centre
CBS	Centraal Bureau voor Statistiek / Central Statistics Netherlands
CIE	Centrum voor Infectieziekten Epidemiologie / Department for Infectious Diseases Epidemiology
COPD	Chronic Obstructive Pulmonary Disease
GGD	Gemeentelijke of Gemeenschappelijke Gezondheidsdienst / Municipal Health Service
IGZ	Inspectie Gezondheidszorg / Health Care Inspectorate
LSI	Laboratorium Surveillance Infectieziekten / Laboratory Surveillance Infectious Diseases
LIS	Laboratorium voor Infectieziekten diagnostiek en Screening / Diagnostic Laboratory for Infectious Diseases and Perinatal Screening
LMR	Landelijke Medische Registratie / National Medical Registration
MEC-TNO	Medical Ethical Committee TNO /Medisch Ethische Commissie TNO
NSCK	Nederlands Signalerings-Centrum Kindergeneeskunde/ Netherlands Paediatric Surveillance Centre
RIVM	Rijksinstituut voor Volksgezondheid en Milieu/ National Institute of Public Health and the Environment
PCR	Polymerase Chain Reaction
PEA	Provinciale Entadministratie / Provincial Vaccination Administration
SAS	Statistical Analysis Computer Program
SIG	Stichting Informatiecentrum Gezondheidszorg / Foundation Information Centre for Health Care
SOP	Standard Operating Procedure
TNO	Nederlandse Organisatie voor Toegepast-Natuurwetenschappelijk Onderzoek /Netherlands Organisation for Applied Scientific Research

Contents

Samenvatting

Inleiding. In 1996-1997 werd in Nederland een plotselinge toename van kinkhoest waargenomen waaronder een relatief groot aandeel recentelijk gevaccineerden. Onze surveillance gegevens suggereerden een daling van de vaccin-effectiviteit maar deze schattingen moeten met voorzichtigheid worden geïnterpreteerd omdat gevaccineerden een milder ziektebeloop hebben. Meer inzicht is nodig in de ernst van kinkhoest gestratificeerd naar de vaccinatiestatus en de leeftijd.
Methoden. In 1997 werden gegevens verzameld van ziekenhuisopnamen ten gevolge van kinkhoest met behulp van de pediatrische surveillance van de Nederlandse Vereniging van Kindergeneeskunde (NSCK). De gegevens werden vergeleken met de nationale gegevens over ziekenhuisopnamen om de dekkingsgraad te berekenen. Daarnaast werden in het Aangifte-plus onderzoek additionele gegevens verzameld van aangegeven kinkhoestgevallen bij de Inspectie van de Gezondheidszorg met behulp van een vragenlijst. In beide studies werd de vaccinatiestatus gevalideerd.
Resultaten. Er werden gegevens verzameld van 180 ziekenhuisopnamen, ongeveer de helft van alle ziekenhuisopnamen in 1997 ten gevolge van kinkhoest. Evenveel jongens als meisjes werden opgenomen. De vaccinatiestatus was sterk gerelateerd aan de leeftijd. Van de ziekenhuisopnamen was 42% jonger dan 3 maanden en niet gevaccineerd; 14% was 3-5 maanden oud waarvan 69% incompleet gevaccineerd; 42% was 6 maanden en ouder waarvan 70% gevaccineerd en van 26% was de vaccinatiestatus onbekend. Bij 53% werd de diagnose bevestigd door positieve kweek of PCR en bij 44% door positieve serologie. Twee kinderen van 3 weken oud zijn overleden. Convulsies (3%), atelectase (1%) en encephalopathie (1%) kwamen alleen voor onder erg jonge ongevaccineerde kinderen. Jonge ongevaccineerde kinderen hadden in vergelijking met gevaccineerde kinderen significant vaker episodes van cyanose (77% vs. 40%) en apneu (22% vs. 5%) en waren langer opgenomen (mediaan 12 vs. 5 dagen). Andere klassieke symptomen verschilden niet significant. In het Aangifte-plus onderzoek werden van 507 gevallen aanvullende gegevens verzameld, ongeveer 50% van het totaal aantal aangiften in de onderzoeksperiode. Zes procent was jonger dan 1 jaar; 36% 1-4 jaar; 28% 5-9 jaar; 10% 10-14 jaar; 21% 15 jaar en ouder. Slechts 7% was ongevaccineerd waarvan 27% jonger dan 3 maanden en 36% 16 jaar en ouder; 2% was onvolledig gevaccineerd; 80% was gevaccineerd; van 11% was de vaccinatiestatus onbekend. Vier procent van de cases werd bevestigd door positieve kweek of PCR en 83% door positieve serologie. Alleen in de oudere leeftijdsgroep hadden meer vrouwen (68%) dan mannen (32%) deelgenomen. Paroxysmaal hoesten (93%), braken (78%), kinken (67%) en ademnood (61%) werden het vaakst gerapporteerd. Ongevaccineerden ten opzichte van gevaccineerden jonger dan 16 jaar hadden significant vaker cyanose (43% vs. 21%) en stille aanvallen (24% vs. 8%) en werden vaker in het ziekenhuis opgenomen (38% vs. 3%). Onder de aangiften van 16 jaar en ouder werden minder ernstige complicaties gerapporteerd in vergelijking met de jongere leeftijdsgroep. Bij jonge gevaccineerde kinderen (7 maanden-2 jaar) kwam met name cyanose vaker voor dan bij oudere gevaccineerde kinderen (3-15 jaar). Zowel bij de ziekenhuisopnamen als bij de aangiften werden vaak onderliggende respiratoire aandoeningen gerapporteerd (16% vs. 19%). De kans op foutieve registratie van de vaccinatiestatus nam toe wanneer niet werd gevaccineerd volgens het vaccinatieschema bijv. wegens het doormaken van kinkhoest.
Conclusie. Ernstige kinkhoest met ziekenhuisopname kwam met name voor bij ongevaccineerden kinderen jonger dan 3 maanden. Echter, ziekenhuisopname was ook nodig bij recent gevaccineerde kinderen maar het klinisch beeld was minder ernstig. Hoewel het klinisch beeld van kinkhoest bij de aangiften beïnvloed werd door de aangiftecriteria, concluderen we dat zelfs onder gevaccineerde kinderen klassieke kinkhoest voorkomt maar ernstige kinkhoest met complicaties is onwaarschijnlijk. Het effect van vaccinatie onafhankelijk van leeftijd kon niet worden bestudeerd omdat slechts enkele ongevaccineerden ouder waren dan 6 maanden. Om deze reden kon op grond van deze beschrijvende studie geen vaccin effectiviteit worden geschat. Echter, een verschuiving naar een minder ernstig ziektebeeld lijkt niet waarschijnlijk en is een werkelijke daling van vaccin-effectiviteit aannemelijk.

Summary

Introduction. In 1996-1997, a sudden increase of pertussis was observed in the Netherlands, with a relatively high proportion of cases in recently vaccinated cohorts. Our surveillance data suggest a decrease in vaccine-efficacy, but estimation from surveillance data should be interpreted with caution. Vaccinated individuals are expected to have less severe disease but it was impossible to differentiate the vaccine-efficacy according to the severity of disease. Therefore, more insight into the disease severity according to vaccination status is needed among hospitalised and notified cases.
Methods. In 1997, data of hospitalisations were collected through the 'Dutch Paediatric Surveillance Centre' (NSCK) and compared with the routine national registration of pertussis hospitalisations to estimate the coverage. Besides, additional data of notified cases were obtained through a questionnaire. In both studies, the vaccination status information was verified from various sources.
Results. Data of 180 hospitalisations were collected covering about half of all pertussis hospitalisations. Vaccination status was strongly related with age. Forty-two percent was younger than 3 months of age and not vaccinated; 14% was 3-5 months of age of whom 69% incompletely vaccinated; 42% was 6 months and older of whom 70% vaccinated and 26% with an unknown vaccination status. Fifty-three percent was confirmed by positive culture or PCR and 44% by positive serology. Two infants, 3 weeks of age, died. Convulsions (3%), atelectasis (1%) and encephalopathy (1%) occurred only among the very young unvaccinated infants. Young unvaccinated compared to vaccinated children had significantly more frequently episodes of cyanosis (77% vs. 40%) and apnoea (22% vs. 5%) and were longer hospitalised (median 12 days vs. 5 days). Other classical symptoms did not differ. Gender was equally distributed. Additional data were collected from 507 notified cases, which is about 50% of all the cases notified during the study period. Six percent was younger than 1 year of age; 36% 1-4 year; 28% 5-9 year; 10% 10-15 year; 21% 16 years and older. Only 7% was unvaccinated of whom 30% less than 3 months and 36% 16 years and older; 2% was incompletely vaccinated; 80% was vaccinated; 11% had an unknown vaccination status. Four percent was confirmed by positive culture or PCR and 83% was confirmed by positive serology. The gender distribution differed only in the older age group (32% male, 68% female). Overall, most frequently reported symptoms were paroxysmal cough (93%), vomiting (78%), whooping (67%) and shortness of breath (61%). Unvaccinated compared with vaccinated children less than 16 years of age reported only significantly more frequently cyanosis (43% vs. 21%), silent attacks (24% vs. 8%) and hospitalisations (38% vs. 3%). Cases of 16 years and older reported less severe complications compared with the younger age group. Within the vaccinated children, the young (7 months-2 year) suffered more frequently from cyanosis than the older children (3-15 years). A high frequency of underlying respiratory disorders was found among hospitalised cases (16%) and notified cases (19%). Inaccurate reporting of the vaccination status was increased when the normal vaccination schedule was interrupted because of e.g. pertussis.
Conclusion. Serious morbidity leading to hospitalisation was mainly reported in young unvaccinated infants less than 3 months of age. Yet, hospitalisation also occurred in recently vaccinated children but the clinical picture was less life threatening. Although the clinical picture of pertussis in the notified cases was influenced by the criteria for notification, with a bias towards severity, we conclude that even among vaccinated children classical pertussis occurs but very severe illness with complications is unlikely. Adults had similar symptoms compared with notified children, but complications were less severe. The effect of vaccination independent of age could not be studied, as only a few unvaccinated cases were more than 6 months of age. Therefore, from this descriptive study no reliable estimate of vaccine-efficacy can be made. We discussed however, that no change towards a less severe clinical picture is plausible and therefore it seems that the decrease in vaccine-efficacy observed from surveillance data (1994-1996) reflects a true decrease.

Outline of the report

In this report, the results of the paediatric surveillance and the notification studies are reported on severity of symptoms due to pertussis in relation to the vaccination status and age. The main reason to collect data about the severity of disease was the increasing incidence of pertussis since 1996. As a consequence of describing two studies in one report we realize a great amount of data is presented. To make the report more easy to read or to limit reading to specific parts in which the reader is interested, we summarize below the outline of the report.

- ***Chapter 1*** is the introduction including the background and main objectives of the studies.
- The paediatric surveillance is described in ***chapter 2*** starting with the methods used to collect clinical data and vaccination information of the cases registered in the paediatric surveillance (*2.1.1* to *2.1.2*). Paragraphs *2.1.3* and *2.1.4* describes the methods used to compare our data with the national data about hospital admission. Results about the response and representativeness of the paediatric surveillance compared with national data are described in paragraphs *2.2.1* to *2.2.4*. Detailed results about the vaccination status, diagnosis, symptoms and underlying disorders of the hospitalized cases in the paediatric surveillance are described in *2.2.5-2.2.8*.
- ***Chapter 3*** describes the notification study starting with the methods used to collect data in the notification study (*3.1.1* to *3.1.3*). In *3.1.4* the method is described about the comparison between the data of the notification study with the data in the routine notification system. Results about the response, the representativeness and the general characteristics of the notification study are described in paragraph *3.2.1* to *3.2.4*. The paragraphs *3.2.4* to *3.2.11* deals with the detailed results about the vaccination status, diagnosis, underlying disorders, transmission and clinical symptoms of the notified cases.
- The findings of a validation study on the vaccination status are described in ***chapter 4***. A prerequisite for classification of the cases into different vaccination status groups was reliable information about the vaccination status. Therefore, we collected this information from different health centres and compared the vaccination status registered by the different health centres between each other (*4.1.1*). In addition, results are described of the validation of the vaccination status reported in the routine notification system (*4.1.2*). Results are described in paragraph *4.2*.
- In ***chapter 5*** the results of the studies are discussed ordered by the main subjects as described in chapter 2, 3 and 4.
- Finally, in ***chapter 6***, general conclusions and recommendations for further studies are given.

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1. Introduction

1.1 Clinical features of pertussis

Pertussis (whooping cough, cough of 100 days) is one of the most communicable respiratory diseases. It is caused by the bacteria *Bordetella pertussis* or (less commonly) *Bordetella parapertussis*. Although most infections are described in unvaccinated infants and children, they can also occur in vaccinated children and adults (1,2,3). Three clinical stages are recognised in case of classical pertussis: catarrhal, paroxysmal and convalescent lasting in total 6 to 8 weeks or longer, depending on the patient's age and immunisation status (1,4). The catarrhal stage, lasting 1 to 2 weeks, is characterised by non-specific upper respiratory symptoms such as mild cough and rhinorrhoea. In this first stage the disease is most contagious and isolation of *B. pertussis* is most likely to be successful. The paroxysmal stage is the longest of the three and may last from 2 weeks up to 1 month or even longer. The mild cough increases in frequency and severity. The paroxysmal cough is followed by a forceful inspiratory effort causing the characteristic whoop. These paroxysms may be accompanied by other symptoms such as apnoea, cyanosis and vomiting. In the last convalescent stage the coughing paroxysms decrease in frequency and severity. Especially in very young patients (0-5 months) pertussis can be dangerous with severe complications such as secondary pneumonia, convulsions and encephalopathy requiring hospitalisation. In these infants the case-fatality rate is approximately 1%. During the 1992-1993 epidemic in the United States three fourths of the infants who died were too young to be vaccinated (5). The clinical course in immunised children is often described as milder than in unimmunised children, while infection with *B. pertussis* in adults is usually not even diagnosed (3,6).

1.2 Surveillance and epidemiology of pertussis

The introduction of killed whole-cell pertussis vaccine in 1952, strongly decreased the incidence and mortality of pertussis in the Netherlands. Children were vaccinated at the age of 3, 4, 5 and 11 months with a diphtheria, tetanus, pertussis and inactivated polio vaccine (DTP-IPV). Protection by vaccination can only be expected after 3 vaccinations, thus at 6 months of age. Recently, in 1999, the vaccination schedule is changed to 2, 3, 4 and 11 months of age. Since 1976 notification of pertussis is obligatory by law, but only in 1988 a strict case definition for pertussis was introduced (Appendix II). From the eighties the Diagnostic Laboratory for Infectious Diseases and Perinatal Screening (Dutch acronym: LIS) almost exclusively performed the serological tests for the confirmation of pertussis in the Netherlands. Furthermore, all isolates of *B. pertussis* from the regional laboratories for public health are serotyped at the RIVM in the Laboratory Surveillance Infectious Diseases project (LSI). Since 1905, the Central Bureau for Statistics (CBS) registers deaths due to pertussis. Data on hospital admissions due to pertussis are available at the National Medical Registration (LMR) of the Foundation Information Centre for Health Care (SIG) with a coverage of 99% of all hospitalisations in the Netherlands (7).

Until the eighties, the incidence of pertussis seemed very low, because cases were reported incidentally. However, in the last two decades pertussis remained endemic. This is surprising in view of the fact that the vaccination coverage for three doses has been high (96,9% at the age of 12 months) (8). Since the introduction of the case definition (see above), increased incidence has been observed in 1989 and 1993/1994. This pattern seemed to be consistent with epidemic peaks every 3 to 4 years such as observed in other countries (9,10,11). However, in 1996, an unexpected increase of notifications (2771 in 1996 compared to 319 in 1995), positive serodiagnoses and hospital admissions of pertussis were observed. This is very likely to reflect a true increase in pertussis incidence. It was established that a higher awareness, improved surveillance, changes in diagnostic practice or a lower vaccine coverage could not explain the epidemic (12,13). Interestingly, the re-emergence of pertussis is associated with the expansion of strains, which are antigenically distinct from the vaccine strains (14). Studies to explain the unexpected course of pertussis in the Netherlands, among others further molecular biological research, are still in progress.

Since the increase of pertussis was the strongest for 1-10 year old vaccinated children, the surveillance data suggest a decrease in vaccine efficacy estimated by the screening method for notification data (13). However, the estimated vaccine efficacy should be interpreted with caution as it has been reported that pertussis is more severe in unimmunised children than in immunised children (15,16). The calculated vaccine efficacy could be underestimated when the severity of disease is not taken into account. Therefore, estimations of vaccine efficacy have to be stratified by severity of disease. During the epidemic, the ratio of hospital admissions to notifications among infants less than one year was comparable to previous years. Although this indicates that the severity among young infants did not change, more clinical information of cases is needed to verify the severity of pertussis in order to reconsider the efficacy of the whole cell vaccine. It is especially important to have information on the severity of the disease in relation with the vaccine history in young infants. Protection of these most vulnerable infants is the main reason for national pertussis vaccination.

Therefore, in 1997 two descriptive studies were conducted on the severity of pertussis in hospitalised children and in notified cases. Data on hospitalised children were collected through the 'Dutch Paediatric Surveillance Centre' (NSCK). Additional data of notified cases were obtained through a questionnaire, which was linked to the regular system of notifications. An important disadvantage was studying a selected group by notification. Therefore, a case-control study was suggested with laboratory confirmation in both cases and controls. Unfortunately, such a study design appeared to be not feasible for various reasons. To estimate the coverage of the NSCK study, our data were compared with the national data. Both in the NSCK and in the notification study, the vaccination status information was verified from various sources. In this report, the results of both studies are described in detail.

1.3 Objectives

Paediatric Surveillance

Objective:

1. Describe the severity of pertussis in relation to the vaccination status and age among hospitalised cases due to pertussis.
2. Assess the total number of hospital admissions due to pertussis in 1997 and calculate the NSCK coverage in comparison with the nation-wide hospital admissions.

Questions:

1. What are the clinical symptoms, age, method of laboratory confirmation and vaccination status of hospitalised cases?
2. Which possible risk factors are related with a severe clinical course of pertussis?
3. What is the incidence, age- and gender distribution of the total hospital admissions due to pertussis in 1997?
4. What is the coverage of the hospital admissions reported by the paediatric surveillance in comparison with the nation-wide hospital admissions data of the Foundation Information Centre for Health Care (SIG)?

Notification study

Objective:

Describe the severity of pertussis in relation to the vaccination status and age among notified cases.

Question:

1. What are the clinical symptoms, age, method of laboratory confirmation and vaccination status of notified cases?

Validation of vaccination status

Objective:

Validation of the vaccination status of both hospitalised and notified cases.

Question:

1. Is the vaccination status information reported by various health centres equivalent?
2. Is the vaccination status registered in the routine notification system equivalent with the verified vaccination status?

2. Paediatric surveillance

2.1 Methods

2.1.1 Netherlands Paediatric Surveillance Centre

In 1997, an active surveillance of pertussis among hospitalisations was carried out in paediatric practice through the NSCK. The formation of this centre was an initiative of the Netherlands Paediatric Association (NVK) and was co-ordinated by TNO Prevention and Health (Dr. RA Hirasing). Monthly, a number of rare disorders were reported and in 1997 91% of all practising paediatricians participated (17). All practising physicians received a card on which the disorders were listed. They were asked to tick off every disorder that they observed for the first time (new case) during the last month and to state the patients initials and date of birth. If they did not see any of the disorders listed, they had to tick off 'no observation'. In either way, the card had to be sent back to the NSCK. The cases reported to the NSCK had to meet the following case-definition: *hospital admission due to suspicion of pertussis*. Positive reactions were passed to our investigators, who subsequently started additional data collection through a questionnaire (see appendix III). In this manner, further information on clinical, diagnostic and vaccination status was obtained (see figure 2.1). If the paediatrician did not respond within 3 to 4 weeks, he or she was reminded by telephone to return the questionnaire. For analyses only cases that were admitted to the hospital in 1997 were included. The NSCK surveillance has been continued in 1998.

Case definition NSCK: hospital admissions due to suspicion of pertussis in 1997

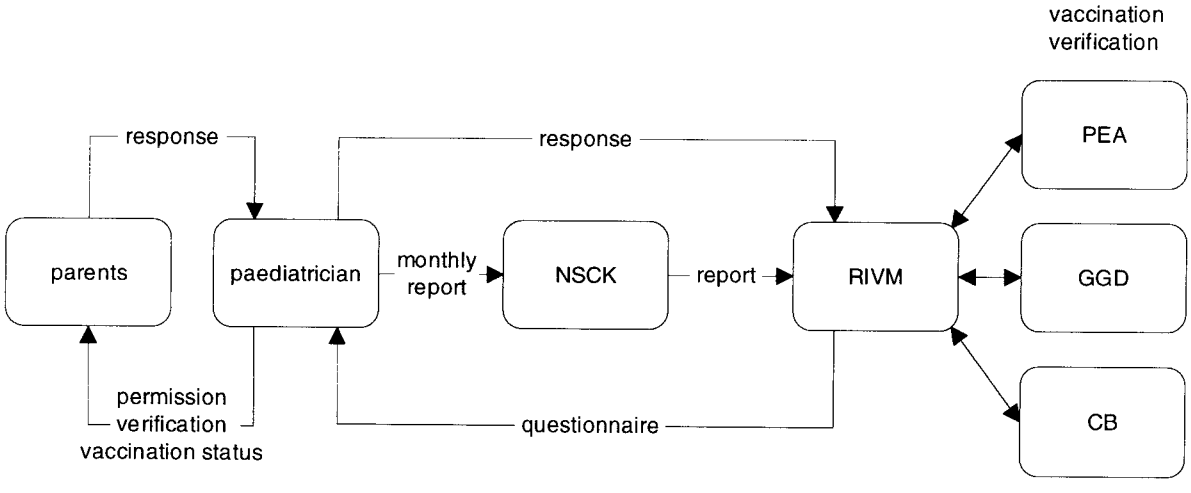

Figure 2.1 Scheme of the NSCK surveillance system

2.1.2 Verification and definition of the vaccination status

To collect complete data about the vaccination status, the paediatrician asked the parents of the patient for permission to verify the vaccination status at various agencies. The written informed consent (appendix IV) was sent to the RIVM. The investigators subsequently passed these informed consents and questionnaires (see appendix V) to the Provincial Vaccination administrations (PEA), the Child Health Centres (CB) and/or the Municipal Health Services (GGD) depending on the age of the patient. Thus, information about the vaccination status including the number of pertussis vaccinations and the day/month/year (PEA only month/year) on which the vaccinations were administered were available from various public health centres and compared with each other (see results chapter 4).

The vaccination status used for analyses was classified according to the information from the highest-ranking source. The following hierarchy was used: CB, GGD, NSCK (paediatrician), and PEA. Thus for example, if there was vaccination information available at the CB, the vaccination status used for the analyses was based on this information. Otherwise, if no information was available at the CB, the GGD information was used etc. Vaccinations administered after the first day of illness were not included to determine a patient's vaccination status. For analysis a patient was considered to be unvaccinated in case: 1) information was not available at any agency and the paediatrician confirmed the patient was not vaccinated; 2) the patient was younger than 3 months of age; 3) all vaccines administered did not include the pertussis component according to the record. A patient was classified as incompletely vaccinated when records were available showing 1 or 2 doses with a pertussis component were administered. The classification vaccinated was used for patients whom received 3 or 4 doses of the pertussis vaccine according to the record. A patient was classified as unknown if no detailed vaccination information (month/year and type of vaccination) was available and if the patient was at least 4 months of age.

Vaccination status	
unvaccinated	no information from public health centres and confirmation paediatrician or younger than 3 months of age or no pertussis component in vaccine
incompletely vaccinated	1 or 2 doses
vaccinated	3 or 4 doses
unknown	no detailed information available from any source

All data collected were entered twice using Epi Info (version 6.04) by two investigators. Differences were checked and corrected. For analysis all data were converted to SAS-data using DBMS-copy. The analyses were performed using the Statistical Package SAS (version 6.12).

2.1.3 National hospital admission data

Information about all hospital admissions with a primary or secondary diagnosis of pertussis (International Classification of Diseases Ninth revision, Clinical Modification code: 0330-0339) in 1997 was provided by the Foundation Information Centre for Health Care (SIG). The following identifiers were available for each patient: code of diagnosis, gender, age (months or years), code of residence, name of residence, date of admission and date of discharge. For privacy reasons the SIG provided no data on patients' names and date of birth. For 1997 the SIG included only those hospitalisations with day of discharge in 1997. Age was calculated at the date of admission. The data were retrieved as an ASCI-file and converted to SAS-data using DBMS-copy. The analyses were performed using the Statistical Package SAS (version 6.12).

2.1.4 Linkage of the paediatric surveillance data with national hospital admission data

An estimation of the degree of underreporting was calculated by the overall method: number of cases in the NSCK compared to the number of cases in the SIG. Besides, cases were primarily linked using age, gender, place of residence, date of hospital admission and date of discharge (see appendix VI). Taken into account the restricted age range of the NSCK surveillance, only SIG data of patients aged 0-14 years were linked. The SAS-data were converted to Microsoft Excel-files using DBMS-copy. Linkage was performed using Microsoft Access 97 SR1.

2.2 Results

2.2.1 Response of the paediatric surveillance

Table 1 shows that in 1997 paediatricians reported 230 cases of suspected pertussis in hospitalised children to the NSCK. According to the paediatricians five cases did not meet the NSCK case-definition (no pertussis diagnosed later on) and 21 cases were reported twice. Of 24 cases no questionnaire was returned after the initial report of the paediatricians to the NSCK. Of 180 reports the paediatrician returned the questionnaire. The first day of illness was unknown in 3 cases. In these cases, the mean time between first day of illness and day of hospital admission was used to estimate the first day of illness. The onset of illness was in 1996 for 13 cases and in 1997 for 167 cases. Sixty-two percent of the 180 cases returned an informed consent to verify the vaccination status. Gender was equally distributed.

Table 2.1 NSCK reports of pertussis in 1997

reports	number (%)
total reports	230 (100%)
duplicates	21 (9%)
false report	5 (2%)
no questionnaire returned	24 (10%)
questionnaire returned	180 (78%)
questionnaire returned (n=180)	
first day of illness in 1996	13 (7%)
first day of illness in 1997	167 (93%)
informed consent to obtain the vaccination status	112 (62%)
gender (n=180)	
male	90 (50%)
female	90 (50%)

2.2.2 National hospital admission data and coverage paediatric surveillance

Table 2.2 shows that the national number of hospital admission registered by the SIG was 480 in 1997 (younger than 15 years). Gender was equally distributed. In 423 cases (88%) pertussis was the primary diagnosis. In 57 cases (12%) pertussis was the secondary diagnosis. In case pertussis was the secondary diagnosis, no information was obtained about the primary diagnosis. The median duration of hospitalisation was 7 days but varied widely from 0 to 71 days. Because het NSCK registered 204 cases and the SIG 480, the estimated NSCK coverage is 43%. Linkage of the NSCK with the SIG was only performed for children younger than 15 years of age (appendix VI). Figure 2.2 shows that linkage was possible in 130 cases. The SIG registered in 121 cases pertussis as primary diagnosis and 9 cases as secondary diagnosis. Fifty NSCK cases could not be linked with the SIG data. Twenty-four individuals could not be linked because there was no questionnaire information available in the NSCK system.

Table 2.2 Characteristics of cases reported by the SIG in 1997

characteristics	number (%)
total number of hospital admissions < 15 years of age*	480 (100%)
gender	
male	229 (48%)
female	251 (52%)
diagnosis	
primary	423 (88%)
secondary	57 (12%)
median number of days of hospital admission (range)	7 (0-71)

* 18 hospital admissions >= 15 years of age were excluded

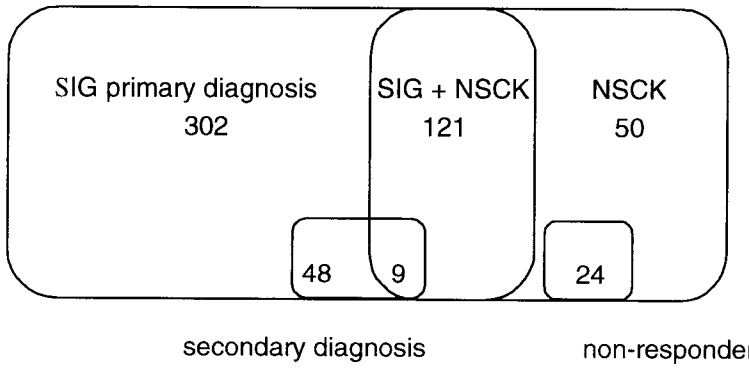

Figure 2.2 Coverage of NSCK compared to national data reported by the SIG in 1997

2.2.3 Age distribution of cases in the paediatric surveillance and the national hospital admission data

The age distribution among the NSCK cases and the SIG cases is shown in figure 2.3. For comparison, age was calculated by the time between the date of birth and the date of hospital discharge. For 5 cases in the NSCK system the day of discharge was missing. Overall, in the age group less than 1 year the proportion of hospital admissions decreases rapidly between 2 to 5 months of age. Most of the cases are younger than one year (67%) and 46% is younger than 3 months. The distribution of age in the NSCK data was comparable with the SIG data.

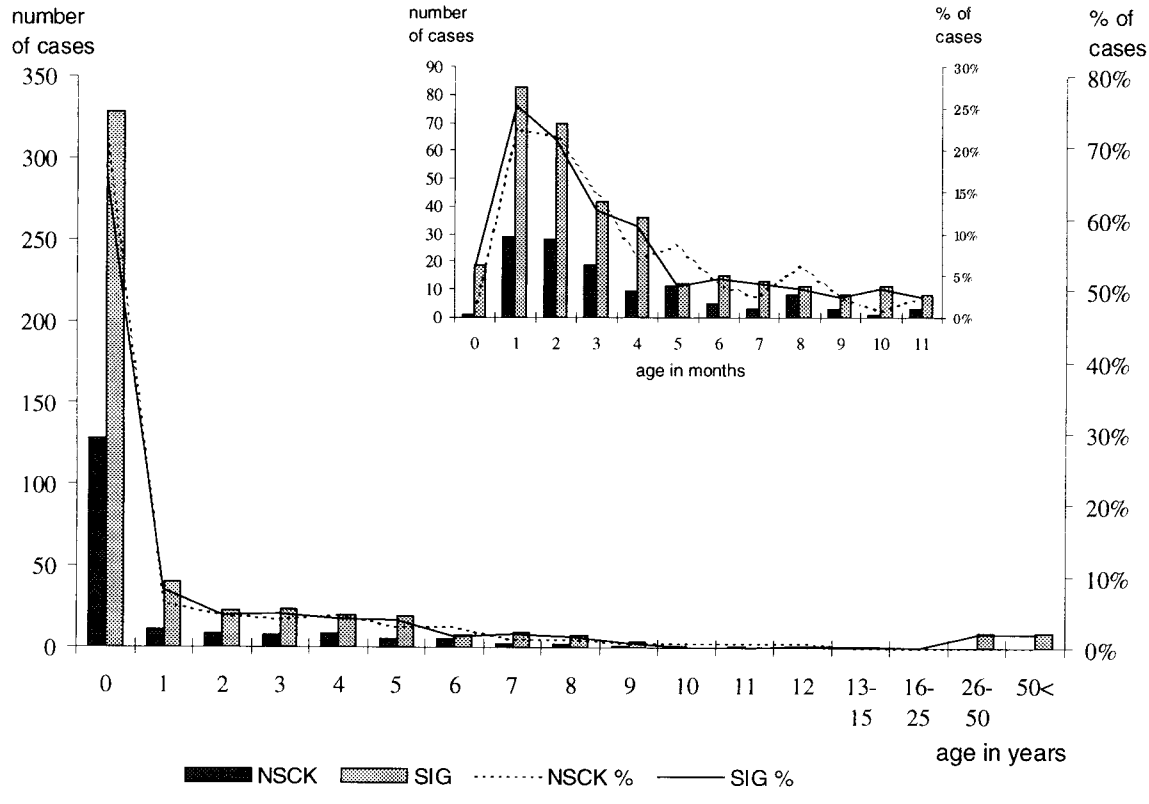

Figure 2.3 *Age distribution of pertussis cases reported by the NSCK (n=180) compared with cases reported by the SIG (n=480)*

2.2.4 Vaccination status of the cases in the paediatric surveillance

Table 2.3 presents the vaccination status of the NSCK cases according to the vaccination records of the CB, GGD, PEA and the paediatricians. Forty-four percent of the cases were unvaccinated. This was due to the fact that the majority of the cases were observed in very young infants. Six percent received 1 dose and another 6% 2 doses. One third of the cases received 3 or 4 doses (30%). In 14% of the cases no information about the vaccination status could be obtained at all.

Table 2.3 Vaccination status of NSCK pertussis cases

vaccination status	Number (%)
not vaccinated	79 (44%)
1 dose	11 (6%)
2 doses	10 (6%)
3 doses	24 (13%)
4 doses	31 (17%)
unknown	25 (14%)
total	180 (100%)

Figure 2.4 shows the distribution of cases according to vaccination status and age. In contrast with figure 2.3, age was calculated by the time between the date of birth and the date of onset of disease. The vaccination status was classified as described in paragraph 2.1.2. All cases younger than 3 months were unvaccinated except 1 case to which the first vaccination was administered a few days before the age of 3 months, according to the CB. Cases aged 6 months and older received mostly 3 or 4 vaccination doses. Fifty-two children were at least 12 months of age and of those, 1 child received no dose, 1 received two doses, 5 received 3 doses, 30 received 4 doses and of 15 children the vaccination status was unknown

Table 2.4 shows the number and proportion of vaccinated children according to age. By excluding the unknown vaccination group, 90.5% was vaccinated at the age of 6 to 11 months. Twenty-one children (91.3%) between 1 to 4 years of age were vaccinated. All children aged 4 to 9 years and older were vaccinated.

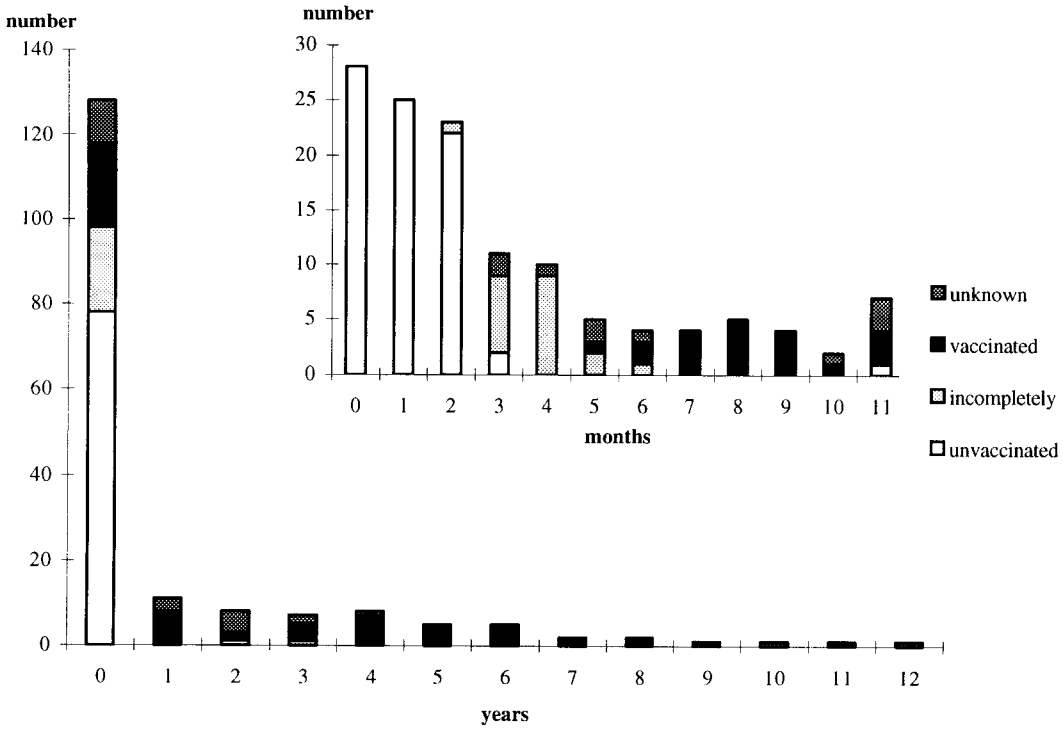

Figure 2.4 NSCK pertussis cases according to vaccination status and age

*Table 2.4 Proportion of vaccinated in NSCK pertussis cases in different age groups**

age	total	unvaccinated / incompletely vac.	vaccinated	proportion vaccinated
0-5 months	97	96	1	1.0%
6-11 months	26	2	19	90.5%
1-4 years	34	2	21	91.3%
5-9 years	15	--	14	100%
10-12 years	3	--	--	--

* persons with unknown vaccination are excluded

2.2.5 Diagnosis of the paediatric surveillance cases

Table 2.5 shows the results of the laboratory diagnosis in which the following hierarchy was used: culture and/or PCR positive, two-point serology, one-point serology, other such as non-conclusive serology, negative microbiological result and unknown diagnostics. Most cases were microbiologically confirmed (53%). In appendix VI the overall results are presented for each method.

Table 2.5 *Laboratory method in hierarchical order* resulting in confirmation of pertussis diagnosis in NSCK cases*

result of laboratory diagnosis	Number (%)
positive culture and/or PCR	96 (53%)
positive two-point serology**	41 (23%)
positive one-point serology**	37 (21%)
other***	6 (4%)
total	180 (100%)

* the method of diagnosis was scored according to the following hierarchy: microbiological, positive two-point serology, positive one-point serology, other result, unknown diagnostic method

** microbiological method not done, negative or missing

*** microbiological method and serological method not done, negative or unknown

2.2.6 Symptoms, complications and duration of the paediatric surveillance cases

Table 2.6 shows that, as expected, the median age of unvaccinated children (one month) and incompletely vaccinated children (four months) is much younger compared with the age of the vaccinated children (19 months) (t-test: $p<0.05$). The median time between first day of illness and the day of hospital admissions was significantly) shorter in unvaccinated children (9 days) compared to vaccinated children (17 days, t-test: $p<0.05$). Furthermore, the median number of days of hospitalisation was longer in unvaccinated (12 days) than in vaccinated children (5 days, t-test: $p<0.05$). In addition, the effect of age was analysed. Children less than three months of age were significantly longer in the hospital and earlier hospitalised than children of three months and older (t-test: $p<0.05$). Other age categories such as younger than 6 months compared with 6 months and older and younger than 1 year compared with 1 year and older showed the same significant differences.

Table 2.6 *Time characteristics (median (range)) of hospitalisation of NSCK pertussis cases according to vaccination status*

characteristics	unvaccinated n=79*	incompletely vac. n=21*	vaccinated n=55*	unknown n=25*	total n=180*
age (months)	1 (0-35)	4 (2-46)	19 (5-113)	16 (3-150)	4 (0-150)
days between onset of illness and hospitalisation	9 (0-49)	11 (2-41)	17 (0-199)	17 (3-103)	14 (0-199)
weeks coughing before hospitalisation	2 (0-26)	2 (1-6)	3 (1-47)	2 (1-12)	2 (0-47)
days hospitalisation	12 (1-44)	11 (1-24)	5 (0-39)	6 (1-25)	8 (0-44)

* the true total number of cases varies due to excluded cases with missing values

Table 2.7 presents the reported symptoms for the pertussis cases for different vaccination groups. Coughing (99%), paroxysmal coughing (73%), vomiting (65%) and cyanosis (60%) are reported most frequently in all the vaccination groups. Furthermore, severe symptoms such as cyanosis, apnoea, collapse, convulsions, pneumonia, respiratory insufficiency and encephalopathy are more frequently reported in unvaccinated than in vaccinated children. However, the difference was only significantly for cyanosis and apnoea (Fisher t-test: $p<0.05$) between the unvaccinated and vaccinated children.

Table 2.7 Reported symptoms of pertussis in NSCK pertussis cases according to vaccination status

symptoms	unvaccinated n=79* (%)	incompletely vac. n=21* (%)	vaccinated n=55* (%)	unknown n=25* (%)	total n=180* (%)
coughing	78 (99)	21 (100)	55 (100)	25 (100)	179 (99)
paroxysmal coughing /whooping	58 (73)	17 (81)	38 (69)	18 (75)	131 (73)
vomiting	48 (61)	15 (71)	35 (64)	18 (75)	116 (65)
cyanosis	61 (77)	13 (62)	22 (40)	11 (46)	107 (60)
fever	34 (43)	7 (32)	19 (35)	8 (33)	68 (38)
catarrhal coughing**	23 (32)	6 (32)	22 (42)	3 (14)	54 (33)
wheezy breathing	15 (19)	5 (24)	15 (27)	3 (13)	38 (21)
apnoea	17 (22)	2 (10)	3 (5)	2 (8)	24 (13)
pneumonia	12 (15)	1 (5)	6 (11)	4 (17)	23 (13)
collapse after coughing	3 (4)	--	1 (2)	3 (13)	7 (4)
respiratory insufficiency with artificial respiration	7 (9)	--	1 (2)	--	8 (4)
convulsions	2 (3)	--	--	--	2 (1)
bradycardia	--	1 (1)	--	--	1 (1)
encephalopathy	1 (1)	--	--	--	1 (1)
atelectase	1 (1)	--	--	--	1 (1)
otitis media	--	--	2 (4)	--	2 (1)
other symptoms***	3 (4)	2 (9)	4 (7)	2 (8)	11 (7)
med. highest temp.(range)	38.6 (38-39)	39.3 (39-39.5)	38.6 (38-40.1)	38.7 (38-39)	38.6(38-40.1)

* the true total number of cases varies due to excluded cases with missing values for some symptoms

** total 166 cases

*** other symptoms: no appetite, blood in sputum, headache, wheezing expirium, irritable after feeding

Figure 2.5.a summarises the total number of reported classical pertussis symptoms in the NSCK cases. Paroxysmal coughing with whooping, vomiting and cyanosis are the most frequently reported symptoms.

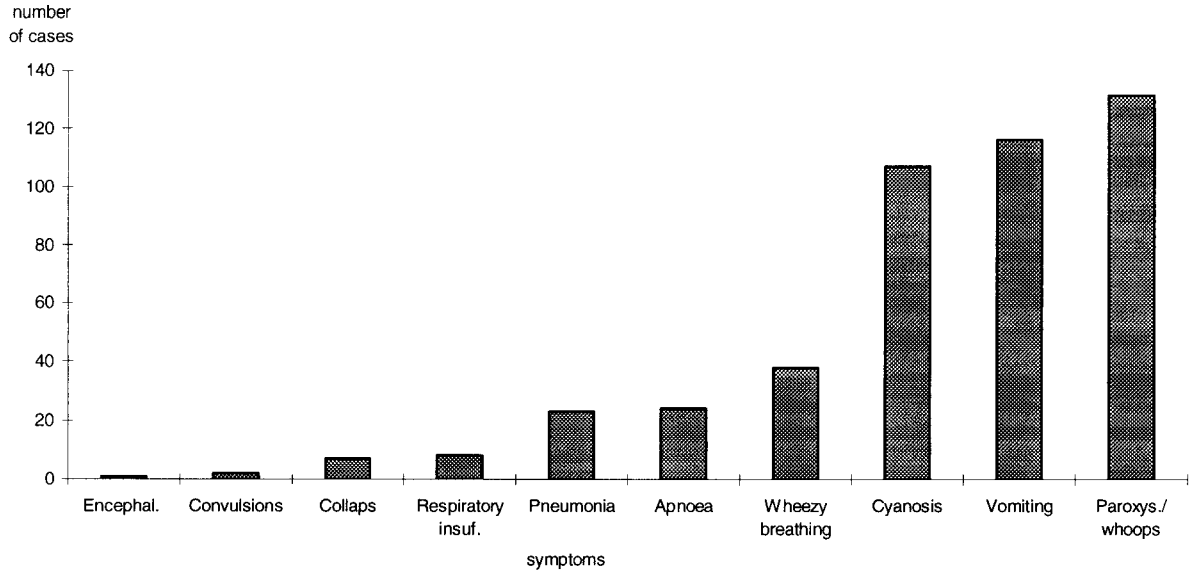

Figure 2.5.a Symptoms in NSCK pertussis cases

Figure 2.5.b shows the same symptoms and complications but now stratified by vaccination status. The most severe complications such as encephalopathy, convulsions, respiratory deficiency, pneumonia, cyanosis and, apnoea are more frequently reported in unvaccinated children. This difference, however, is only significant for cyanosis and apnoea (Fisher t-test: $p<0.05$). The frequency of other symptoms was similar for unvaccinated and vaccinated children.

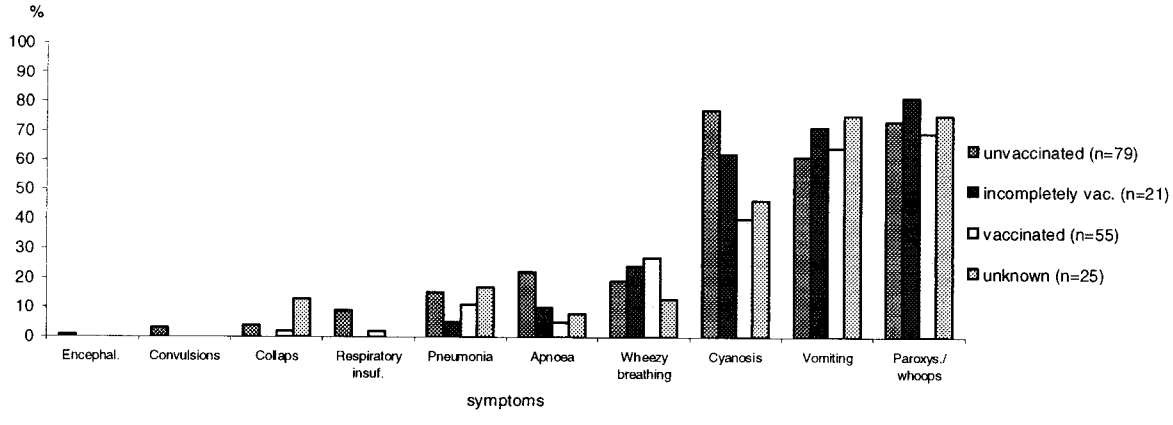

Figure 2.5.b Relative distribution of symptoms in each vaccination group in NSCK pertussis cases (n=180)

Figure 2.5.c shows the frequency of symptoms stratified by age. No clear differences were found between the age groups, except for cyanosis and apnoea (Fisher: $p<0.05$). Within the unvaccinated cases (figure 2.5.d), the typical pertussis symptoms were most frequently reported in the youngest age group (younger than 1 months) compared with those of 1 month or 2 months, however, the differences were not significant except for respiratory insufficiency (Fisher: $p<0.05$). In vaccinated children no consistent age-effect was found although cyanosis was more frequently reported in the younger age group of 3 months to 2 years compared with those of 3 to 15 years (fig 2.5e).

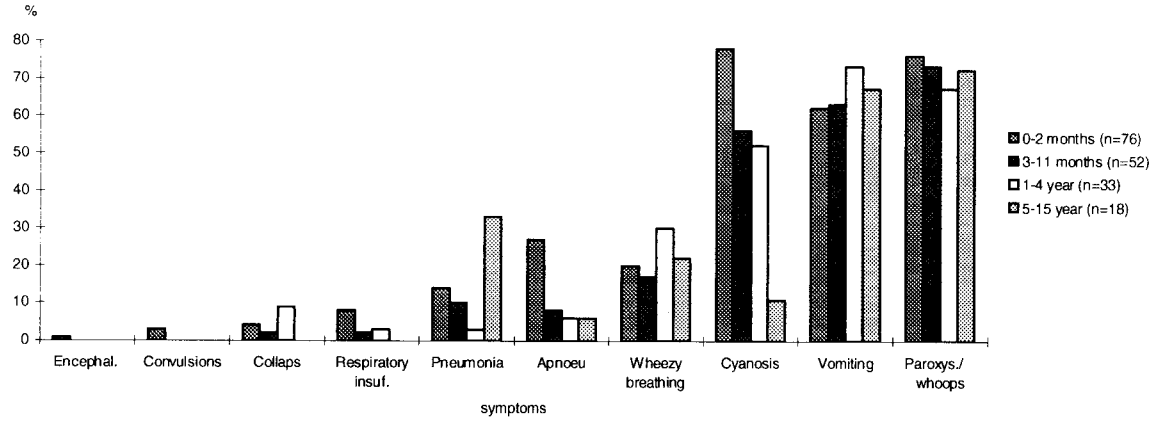

Figure 2.5.c Relative distribution of symptoms in each age group in NSCK cases (n=180)

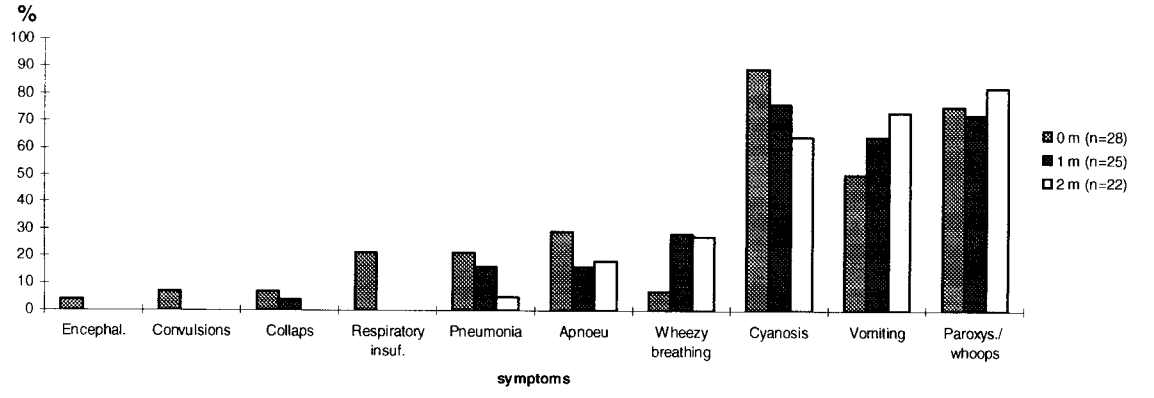

Figure 2.5.d Relative distribution of symptoms in each age group in unvaccinated NSCK cases (n=79)

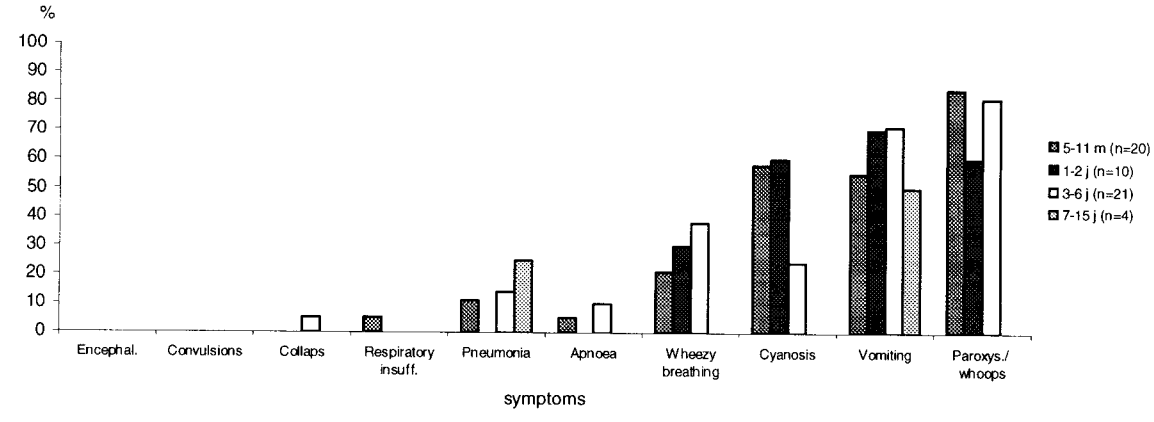

Figure 2.5.e Relative distribution of symptoms in each age group in vaccinated NSCK cases (n=55)

2.2.7 Underling disorders and risk factors of the paediatric surveillance cases

Table 2.8 presents underlying respiratory disorders in the NSCK cases. Most of the reported underlying disorders were COPD, asthma and bronchitis (including bronchial hyperactivity and bronchospasm). In young unvaccinated children only a few underlying disorders were known and therefore reported (1%). In older vaccinated children underlying disorders were frequently reported (34%).

Table 2.8 Reported underlying respiratory disorders in NSCK pertussis cases according to vaccination status

respiratory disorders	unvaccinated n=79 (%)	incompletely vac. n=21 (%)	vaccinated n=55 (%)	unknown n=25 (%)	total n=180 (%)
COPD/asthma/bronchitis	1 (1%)	2 (10%)	18 (34%)	8 (32%)	29 (16%)
adenovirus infection	2 (3%)	--	--	--	2 (1%)
RS bronchiolitis	3 (4%)	--	3 (6%)	--	6 (3%)
bronchopulmonal dysplasia	--	--	3 (6%)	--	3 (2%)
lungdisease after preterm delivery	--	--	1 (2%)	1 (4%)	2 (1%)
wheezing	--	--	--	1 (4%)	1 (1%)

Table 2.9 shows the condition at discharge of the cases. Fifty-nine percent of the unvaccinated were recovered at the moment of hospital discharge, 29% was still coughing and 9% had other symptoms besides coughing. Among the vaccinated cases 38% was completely recovered, 56% was still coughing and, 5% still had other symptoms besides coughing. More vaccinated children than unvaccinated were still coughing at the moment of discharge. According to the NSCK reports, 2 unvaccinated boys, 3 weeks of age, died of pertussis in 1997. In both children pertussis was confirmed by positive culture. No underlying diseases, other infections or preterm delivery were reported. Reported symptoms were apnoea, cyanosis, convulsions and pneumonia. In both cases, oxygen was administered with artificial respiration.

Table 2.9 Reported condition at discharge from hospital in NSCK pertussis cases according to vaccination status

condition at discharge	unvaccinated n=79*	incompletely vac. n=21*	vaccinated n=55*	unknown n=25*	total n=180*
recovered	44 (59%)	13 (65%)	21 (38%)	14 (61%)	92 (53%)
coughing	22 (29%)	4 (20%)	31 (56%)	8 (33%)	65 (37%)
other symptoms besides coughing**	7 (9%)	3 (15%)	3 (5%)	2 (8%)	15 (9%)
died	2 (3%)	--	--	--	2 (1%)

* the true total number of cases varies due to excluded cases with missing values for some symptoms

** other symptoms such as: (paroxysmal) coughing, bronchial hyperactivity, bronchitis, COPD, hypertony, wheezing and dyspnoea

3. Notification Study

3.1 Methods

3.1.1 Notification study

In the period of October 1997 until January 1998 a study was conducted based on the notification of pertussis. The usual procedure for notification is as follows. If a patient meets the case-definition for pertussis (appendix II), every physician has to inform the GGD by means of a card or phone about e.g. the patients name, address, place of residence, date of birth, first day of illness and diagnostic tests. Subsequently, the GGD usually contacts the patient or the parents e.g., to counsel on control measures, to advise vaccination in not or not completely vaccinated contacts and to prescribe chemoprophylaxis. Furthermore, the GGD sends a notification card to the Health Care Inspectorate (IGZ). As part of the study on the severity of pertussis the routine procedure has been expanded. The case-definition for the notification study was: *all new notifications which are registered at the GGD within the period of the first of October 1997 until the end of January 1998 with the first day of illness in 1997.* In general, the GGD's were used to contact the patient after receiving a notification card; thus the GGD informed the patient by (written) information about the study and asked for participation. If the GGD did not contact the patient after notification, the physician informed the patient about the study. If the patient intended to participate, the physician informed the GGD and subsequently contacted the patient. *At least 6 weeks after the first day of illness*, the GGD sent a study questionnaire to the patient. Through this, additional data were collected about the clinical course, the complications and the vaccination status.

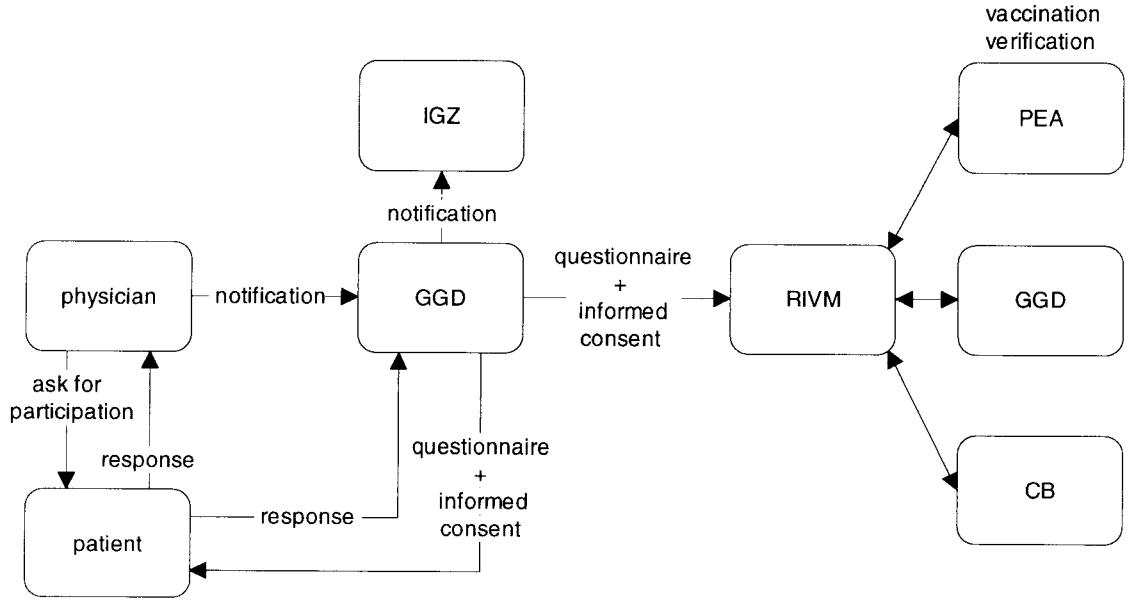

Figure 3.1 Scheme of the notification study

Moreover, the patient was asked to fill in an informed consent (appendix VIII) to verify the vaccination status at the CB, GGD and PEA (forms see appendix V). Verification of the vaccination status was only possible in children younger than 16 years of age. The patient sent the questionnaire, with or without an informed consent, to the GGD. The GGD subsequently forwarded the questtionnaire and the informed consent to the RIVM. In case a patient did not respond within 2 weeks, he/she was reminded by the GGD by telephone (see figure 3.1). Other alternative procedures were also possible depending on the GGD's routine procedure providing that the procedure was in accordance with the conditions of the IGZ.

Case definition:	all new notifications registered at the GGD in the period of the October 1997-January 1998 with the first day of illness in 1997 and filling in the questionnaire at least 6 weeks after the onset of illness.

3.1.2 Questionnaire and fieldwork

The questionnaire is partly based on the NSCK-questionnaire and the PIENTER-questionnaire (18). Two questionnaires had been developed: for patients younger than 16 years of age (appendix IX) and for patients of 16 years and older (appendix X). Six parents of children with pertussis and five GGD's tested the questionnaire. The written information about the study for patients and the information for participating GGD's were tested by these GGD's as well. Before the study started, all participating GGD received background information, examples of letters to inform physicians and patients, copies of informed consents to verify the vaccination status and forms to monitor the fieldwork. The Medical Ethical Committee of the TNO (MEC-TNO) approved the procedures and the questionnaires.

3.1.3 Definition of vaccination status

The definition of the vaccination status is described in paragraph 2.1.2. Only this time the vaccination status information was collected through the questionnaire from parents (instead of paediatricians) using the vaccination certificate. The vaccination status of cases more than 15 years of age could not be verified at the health centres and administrations because they do not hold records of older children. Hence, the vaccination status of older cases was only based on the information collected through the questionnaire using the vaccination certificate although in many cases no vaccination certificate was available. If the patient filled in that he or she was not vaccinated (confirmed with a reason), the patient was considered as not vaccinated. If no reason was given, the vaccination status was defined as unknown. Chapter 4 describes the results of the vaccination status verification.

Vaccination status	
unvaccinated	no information from public health centres and confirmation by notified person with a reason or younger than 3 months or no pertussis component in vaccine
incompletely vaccinated	1 or 2 doses
vaccinated	3 or 4 doses
unknown	no information from any source and no vaccination certificate available

3.1.4 Linkage of the notification study with the routine notification system

Data of notification study and the routine notification system of 1997 were linked to complete the information provided by the patients with data of the laboratory diagnosis. Besides, the registered vaccination status data in the routine notification system were compared with the verified vaccination status and the results are described in chapter 4. Cases from both sources were primarily linked using birth date, name, gender, place of residence (matching procedure appendix XI). Before linkage, the routine notification data were matched with the serology data from the LIS. Thus, of a part of the notified cases the serological basis on which they were notified (one-point/ two-point serology) was also known.

All data collected were entered twice into Epi Info files (version 6.04) by two investigators. Differences were checked and corrected. For analysis all data were converted to SAS-data using DBMS-copy. The analyses were performed using SAS (version 6.12). For linkage the SAS-data were converted to Microsoft Excel-files using DBMS-copy and linkage was performed by using Microsoft Access 97 SR1.

3.2 Results

3.2.1 Participation of the Municipal Health Services

Of all the GGD's (total 51) 46 participated (90%). The reason for not participating was mostly capacity problems within the organisation. The participating GGD's were spread uniformly over the Netherlands, except for the province of Zeeland where no GGD participated.

3.2.2 Response

Table 1 shows the response of the patients. The non-responders (10%) were patients who refused participation when they were asked to participate or patients who did not return the questionnaire. The response did not differ over the age groups (<16 years and >15 years). Of 32 cases the first day of illness was unknown. Nevertheless, this information could be retrieved from the notification system or the serological database in which the day of first illness is included. Cases who did not meet the case definition were excluded: 5 cases became ill in 1996 and 1 case in 1998; one case used a wrong questionnaire; 37 cases filled in the questionnaire to early after onset of disease. In total 507 cases were included: 79% younger than 16 years, 21% older than 15 years. Ninety-five percent of the cases (or parents) younger than 16 years of age returned an informed consent to verify the vaccination status.

Table 3.1 Response of notified pertussis cases and cases excluded

reports	number (%)
total notified patients contacted for participation	613 (100%)
non-response	62 (10%)
response	551 (90%)
cases excluded of the total responders (n=551)	
first day of illness in 1996	5 (1%)
first day of illness in 1998	1 (0.2%)
wrong questionnaire*	1 (0.2%)
<6 weeks interval between first day of illness and filling in the questionnaire	37 (6.7%)
cases included	507 (100%)
questionnaire <16 years	402 (79%)
questionnaire ≥ 16 years	105 (21%)
informed consents verification vaccination status (<16 y)	380 (95%)

* questionnaire ≥ 16 years of age use instead of questionnaire for <16 years of age

3.2.3 Characteristics of the notification study and the routine notification system

Table 3.2 presents general characteristics of the notified cases. In young cases (<16 years) gender was equally divided but in the older age group more women were included (68%). Especially in the older age group, participants often had no vaccination certificate (49%). The median time between the first day of illness and filling in the questionnaire was 11 weeks.

Appendix XII shows the number of the cases in the routine notification system during the 4 months that the study was conducted. Overall, about 1034 cases were notified which is about twice the number of cases who participated. The gender distribution in the notification study was comparable with the distribution in the routine notification system.

Table 3.2 General characteristics notified pertussis cases

characteristics	age <16 years n=402*	age ≥ 16 years n=105*	total n=507*
gender			
male	197 (49%)	34 (32%)	231 (46%)
female	205 (51%)	71 (68%)	276 (54%)
vaccination certificate	370 (95%)	53 (51%)	423 (86%)
median weeks first day of illness and filling in questionnaire (range)	11 (6-49)	11 (6-43)	11 (6-49)
median persons household (range)	4 (1-7)	3 (1-18)	4 (4.2)

* the true total number of cases varies due to excluded cases with missing values

3.2.4 Age distribution of the notification study and the routine notification system

Figure 3.2 shows the age distribution of the notified cases compared with the cases in the routine system notified in the period of October 1997- January 1998. In both systems, age was calculated by the time between the date of birth and the date of the onset of disease. For 195 cases in the routine system the first day of illness was missing and estimated by the mean time between the first day of illness and day of notification which was 67 days. Thus, the first day of illness was estimated by the day of notification minus 67 days. Seventy percent was younger than 10 years, of which most cases 3 to 4 years of age (26%). The proportion of the very young (less than 1 year) was higher in the routine system while the proportion of 4 year old children was higher in the notification study. In the older age group most cases were 30-39 years old (7%). Overall, the age-distribution in the notification study was comparable with routine notification system.

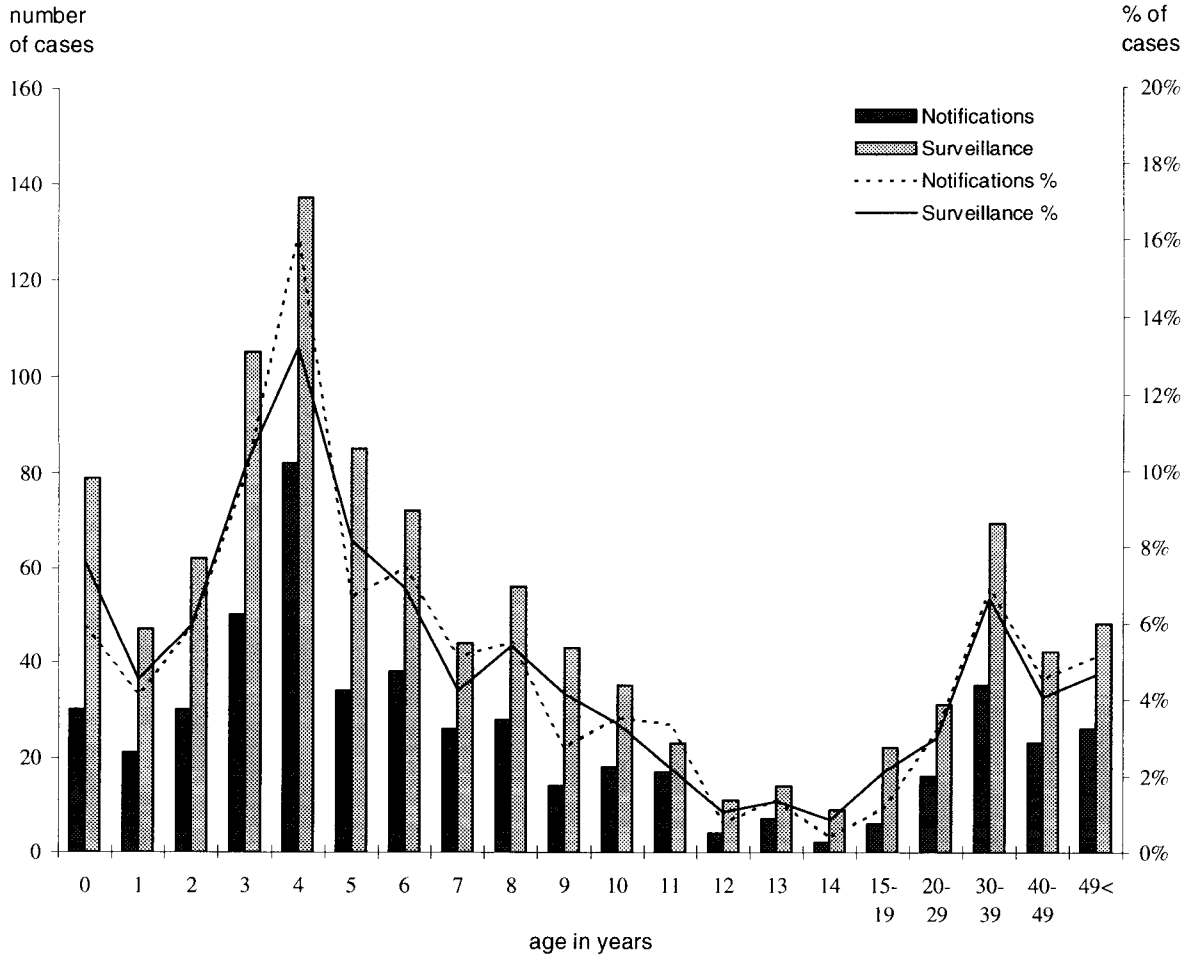

Figure 3.2 *Age distribution of pertussis cases in the notification study (n=507) and the routine system in the period of October 1997 - January 1998 (n=1034)*

3.2.5 Vaccination status of notified cases

Table 3.3 shows that most of the cases were vaccinated. Only 21 children of the cases younger than 16 years were not vaccinated at all of which 9 children were too young to be vaccinated. In the older age group 31% of the cases were completely vaccinated. In 50% of the older cases the vaccination status was unknown. Appendix XII shows the vaccination status of notified cases in the period of October 1997 - January 1998 according to the routine system. Chapter 4 describes the results of the validation of the vaccination status in the routine notification system.

Table 3.3 Vaccination status of notified pertussis cases according to different age groups (n=507)

vaccination status	age <16 years n=402	age ≥ 16 years n=105	total n=507
unvaccinated	21 (5%)	12 (11%)	33 (7%)
1 dose	5 (1%)	2 (2%)	7 (1%)
2 doses	4 (1%)	1 (1%)	5 (1%)
3 doses	21 (5%)	5 (5%)	25 (5%)
4 doses	345 (86%)	33 (31%)	379 (75%)
unknown	6 (2%)	52 (50%)	58 (11%)

* no detailed data about vaccination available, only confirmation from patient

Figure 3.3 shows the distribution of the vaccination status over the different age groups. The vaccination status was classified as described in paragraph 3.1.3. Most of the persons aged 6 months to 24 years old were vaccinated. In adults the vaccination status was often unknown.

Table 3.4 shows the number of vaccinated cases according to age. When the unknown vaccination group was not included 11.1% received at least 3 doses at the age of 0-5 months. In the age group of 6 to 11 months 91.7% received at least 3 doses. Children aged 1 to 4 years and 5 to 9 years were respectively in 99.4% and 97.0% vaccinated. Of children aged 10 to 15 years 89.8% was vaccinated.

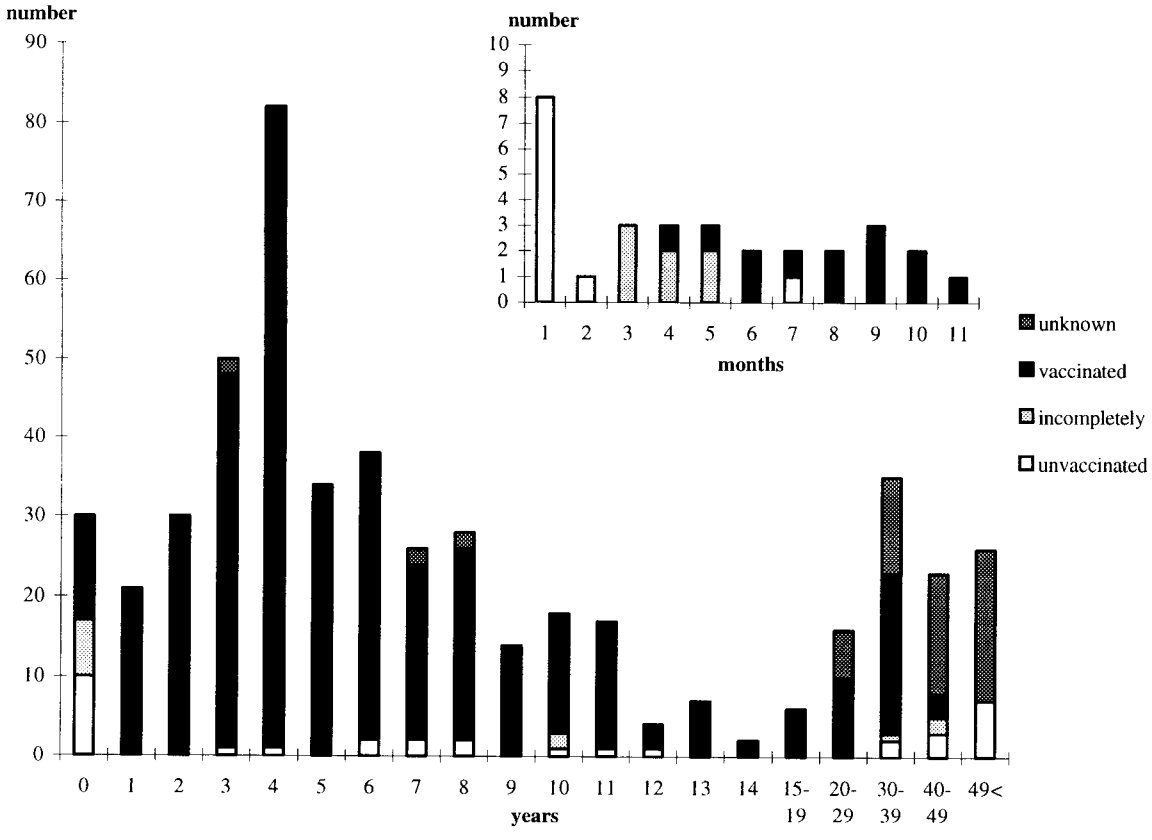

Figure 3.3 *Notified pertussis cases according to vaccination status and age (n=507)*

Table 3.4 *Proportion of vaccinated in notified pertussis cases in different age groups (<16 y)**

age	total	unvaccinated/ incompletely vac.	vaccinated	proportion vaccinated
0-5 months	18	16	2	11.1%
6-11 months	12	1	11	91.7%
1-4 years	183	2	179	99.4%
5-9 years	140	6	130	97.0%
10-15 years	49	5	44	89.8%

* persons with unknown vaccination are excluded

3.2.6 Diagnosis of notified cases

Table 3.5 shows the result of linkage with the routine notification data including the type of diagnosis by which pertussis was confirmed. In 29 cases (6%) no linkage was possible with the notification data. While the notification data were also linked with the serological data (LIS), information was available of 301 cases. Seventy-five cases 75 (15%) were confirmed by two-point serology and 197 (39%) by one-point serology (see also appendix XIII).

Table 3.5 *Method of diagnosis in hierarchical order* from results of matching the notifications with the routine notification database and the serological database by age group*

result of diagnosis	age <16 years n=402	age ≥ 16 years n=105	total n=507
positive culture and/or PCR	19 (5%)	3 (3%)	22 (4%)
positive two-point serology**	64 (16%)	11 (11%)	75 (15%)
positive one-point serology**	153 (38%)	44 (42%)	197 (39%)
positive serology (not matched) **	112 (28%)	35 (33%)	147 (29%)
epidemiological***	15 (4%)	3 (3%)	18 (4%)
other****	18 (4%)	1 (1%)	19 (4%)
not linked	21 (5%)	8 (8%)	29 (6%)

* the method of diagnosis was scored according to the following hierarchy: microbiological, positive two-point serology, positive one-point serology, serological (not matched), epidemiological and other (clinical, method of diagnosis unknown, negative or non-conclusive serology)

** microbiological method not done, negative, or missing

*** microbiological method and serological method not done, negative or missing

**** microbiological method, serological and epidemiological method not done, negative of missing

3.2.7 Underlying disorders of notified cases

Table 3.6 shows that the most reported underlying disorder was COPD (Chronicle Obstructive Pulmonary Disease), asthma or chronicle bronchitis (19%). These disorders were more frequently reported among the children <16 years (21%). Other frequently reported disorders were allergy of the respiratory tract, infection of the nasal, sinus, or pharynx and food allergy. In 54% of the cases no underlying disorders were reported. Thirty children were less than 1 year of age and of those, 5 children were born to early (table 3.7).

Table 3.6 Underlying disorders in notified pertussis cases according to age group

underlying disorders	age <16 years n=402* (%)	age ≥ 16 years n=105* (%)	total n=507* (%)
asthma / COPD / chronic bronchitis	79 (21%)	13 (13%)	92 (19%)
allergy respiratory tract	34 (9%)	12 (12%)	46 (9%)
infection nasal /sinus/pharynx	20 (5%)	7 (7%)	27 (6%)
food allergy	31 (8%)	--	31 (6%)
skin allergy	15 (4%)	5 (5%)	20 (4%)
lung disease other than asthma/COPD/chr.br.	6 (2%)	1 (1%)	7 (1%)
pneumonia	6 (2%)	1 (1%)	7 (1%)
illness of the nervous system	1 (0%)	5 (5%)	6 (1%)
convulsions	4 (1%)	--	4 (1%)
congenital defect	4 (1%)	1 (1%)	5 (1%)
complication after premature delivery	2 (1%)	--	2 (0%)
other illness	56 (15%)	18 (17%)	74 (15%)
no illness	210 (55%)	53 (51%)	263 (54%)

* the true total number of cases varies due to excluded cases with missing values for some disorders

Table 3.7 Prematures in notified pertussis cases less than 1 year

premature	age <1 years n=30 (%)
premature (<38 weeks)	5 (17%)
weeks born to early (n=5) (range)	3 (2.5-7)
median birthweight (n=5) (range)	2910 (2000-4000)

3.2.8 Transmission of notified cases

Participants were asked whether they knew other persons with pertussis symptoms e.g., in their family, neighbourhood or at work. The results are shown in table 3.8. Overall, 191 cases (38%) reported no other pertussis cases, while 299 cases (59%) reported that he/she knew other persons with pertussis. Of those 299 cases, mostly 1 person (45%) or 2 persons (31%) were remembered to have pertussis. Table 3.8 shows also the kind of relation with the contact case. We counted the total number of contacts and then calculated the proportion which were for instance brothers and sisters, parents etc. Especially in the younger age group, brothers or sisters had pertussis (34%) as well. In the older age group, also sons or daughters were often reported to have pertussis (48%). Classmates or colleagues were often reported to have pertussis as well (27%). Within the family, it was difficult to assess whether the other persons were infected before or after the notified case because many times it was unknown.

Table 3.8 Transmission of pertussis in notified cases according to age group

transmission pertussis cases	age <16 years n=402* (%)	age ≥ 16 years n=105* (%)	total n=507* (%)
others with pertussis:			
yes	237 (60%)	62 (59%)	299 (59%)
no	153 (38%)	38 (36%)	191 (38%)
missing	12 (3%)	5 (5%)	17 (3%)
known transmission (n=299)			
1 person	107 (45%)	28 (45%)	135 (45%)
2 persons	74 (31%)	18 (29%)	92 (31%)
3 persons	19 (8%)	8 (13%)	27 (9%)
4 persons	12 (5%)	2 (3%)	14 (5%)
>4 persons	15 (6%)	5 (8%)	20 (7%)
missing	10 (4%)	1 (2%)	11 (4%)
number of persons (mean)	1.26	1.23	1.23
relation with pertussis case*			
brother/sister	34%	2%	27%
parents	10%	4%	9%
son/daughter	--	48%	8%
classmate / colleague	32%	6%	27%
neighbours	10%	8%	10%
family	8%	12%	9%
others	5%	24%	10%

* percentages calculated using the total number of contacts

3.2.9 Symptoms, clinical course and disease impact in notified pertussis cases<16 years

Table 3.9 presents the frequency of coughing or illness at the moment of filling in the questionnaire at least 6 weeks after onset of disease. The number of weeks of coughing or illness was based on the first day of illness. If the patient was still coughing or ill at the moment of filling in the questionnaire then the number of weeks was calculated between the first day of illness and the moment of filling in the questionnaire (in table 3.9 reported as 'symptoms at the moment'). If the symptoms were over then the 'total weeks' have been calculated between the first day of illness and the estimated date when coughing was over. About half of the cases was still coughing at the moment of filling in the questionnaire while 74% was not recovered yet also due to other symptoms. No statistical significant differences were found between the vaccination groups. Table 3.10 shows the number of weeks of coughing and illness, number of times of coughing and duration of coughing. In general, the median number of weeks of coughing was at least eight weeks. The number of times paroxysmal coughing seems to be more frequently reported during the day than the night. The median time with pertussis symptoms was 10 weeks. The median time with symptoms for cases who were still ill at the moment of filling in the questionnaire was 11 weeks. No statistical significant differences were found between the different vaccination groups.

Table 3.9 Number of notified cases with cough and illness at the moment of filling in the questionnaire (≥ 6 weeks after onset of disease) according to vaccination status (<16 y)

	unvaccinated n=21* (%)	incompletely vac. n=9* (%)	vaccinated n=366* (%)	unknown n=6* (%)	total n=402* (%)
paroxysmal coughing total	10 (59%)	4 (50%)	172 (51%)	2 (40%)	188 (51%)
paroxysmal coughing so far	7 (41%)	4 (50%)	164 (49%)	3 (60%)	178 (49%)
symptoms over**	7 (33%)	2 (22%)	92 (26%)	2 (33%)	103(26%)
symptoms at the moment **	14 (66%)	7 (78%)	267 (74%)	4 (67%)	292(74%)

* the true total number of cases varies due to excluded cases with missing values

** symptoms other than coughing

Table 3.10 Duration of coughing and illness, times of coughing and duration of coughing spell in notified cases according to vaccination status (<16 y) (≥ 6 weeks after onset of disease)

duration and times (median (range))	unvaccinated n=21*	incompletely vac. n=9*	vaccinated n=366*	unknown n=6*	total n=402*
weeks parox. coughing total	6 (3-15)	7 (3-12)	8 (1-28)	5 (3-6)	8 (1-28)
weeks parox. coughing so far	10 (7-24)	6 (6-12)	9 (4-24)	12 (8-14)	10 (4-24)
times parox. coughing daily	10 (3-36)	6 (2-10)	8 (1-55)	6 (2-10)	8 (1-55)
times parox. coughing night	7 (4-20)	5 (1-6)	5 (1-48)	5 (4-7)	5 (1-48)
minutes paroxysmal coughing	2 (1-45)	2 (1-10)	3 (1-45)	3 (2-20)	3 (1-45)
weeks symptoms total	13 (1-21)	10 (8-11)	10 (2-22)	7	10 (1-22)
weeks symptoms so far	11 (6-25)	10 (6-16)	10 (6-39)	13(11-25)	11 (6-39)

* the true total number of cases varies due to excluded cases with missing values

Table 3.11 shows that the most frequent symptom was (paroxysmal) coughing. Except 4 cases that were only coughing during the day or night, all others were coughing during the day and night. Two vaccinated cases did not report coughing at all. Vomiting and shortness of breath were equally distributed among unvaccinated compared with vaccinated. On the other hand, whoops, cyanosis, fainting, fever, fever convulsions, weight loss, silent attacks and pneumonia, were more frequently reported among unvaccinated and incompletely vaccinated compared with vaccinated cases although only significantly for cyanosis and silent attacks (Fisher t-test: $p<0.05$). Among the vaccinated other less severe complications such as bleeding tongue and nose, throat infection, were more frequently reported compared with unvaccinated. The symptoms of premature born children did not differ from others.

Table 3.11 Reported symptoms in notified pertussis cases according to vaccination status (<16 y)

symptoms	unvaccinated n=21* (%)	incompletely vac. n=9* (%)	vaccinated n=366* (%)	unknown n=6* (%)	total n=402* (%)
coughing	21 (100)	9 (100)	359 (99)	6 (100)	395 (99)
paroxysmal coughing	19 (91)	8 (89)	345 (96)	5 (83)	377 (96)
vomiting	17 (81)	5 (56)	298 (83)	5 (83)	325 (82)
whooping	15 (79)	5 (63)	240 (70)	3 (60)	263 (70)
shortness of breath	13 (62)	7 (78)	215 (60)	3 (50)	238 (60)
cyanosis	9 (43)	5 (56)	74 (21)	1 (17)	89 (22)
fainting	3 (14)	--	15 (4)	1 (17)	19 (5)
fever	12 (57)	4 (44)	143 (39)	2 (33)	161 (40)
fever convulsions	1 (8)	--	2 (1)	--	3 (1)
weight loss	13 (62)	5 (63)	129 (42)	1 (17)	148 (43)
silent attacks	5 (24)	2 (22)	28 (8)	2 (33)	37 (9)
complications					
pneumonia	3 (15)	1 (11)	16 (5)	--	20 (5)
disease respiratory tract	1 (5)	--	25 (7)	--	26 (7)
otitis media	4 (20)	--	40 (11)	1 (20)	45 (12)
epilepsy	--	--	1 (0)	--	1 (0)
disorder of nervous system	--	--	1 (0)	--	1 (0)
bleeding eye	1 (5)	2 (22)	15 (4)	1 (17)	19 (5)
bleeding tongue	--	--	1 (0)	--	1 (0)
infection throat -/nose	--	--	6 (2)	--	6 (2)
bleeding nose after coughing	--	--	3 (1)	--	3 (1)
muscle pain ribs/shoulders	--	--	2 (1)	--	2 (1)
other complications	--	--	15 (4)	--	--
no complications	12 (60)	6 (67)	244 (69)	4 (67)	266 (68)
median max. temp. (range)	39.5 (38.5-39.8)	38.7 (38.2-39)	39.4 (37.8-41.5)	38.9 (38.8-39)	39.4 (37.8-41.5)
median weight loss(kg)(range)	2 (0.3-4)	1 (0.5-2)	2 (0.3-5)	1 (1)	2 (0.3-5)

* the true total number of cases varies due to excluded cases with missing values for some symptoms

Figure 3.4.a summarises the most frequent or severe symptoms or complications among notified cases younger then 16 years of age as presented in table 3.13. In figure 3.4.b the distribution of each symptom is given per vaccination group. Most symptoms except for paroxysmal coughing, vomiting and shortness of breath are more frequently reported among unvaccinated and incompletely vaccinated compared with the vaccinated. However, those differences were not statistically significant except for cyanosis and silent attacks as described before.

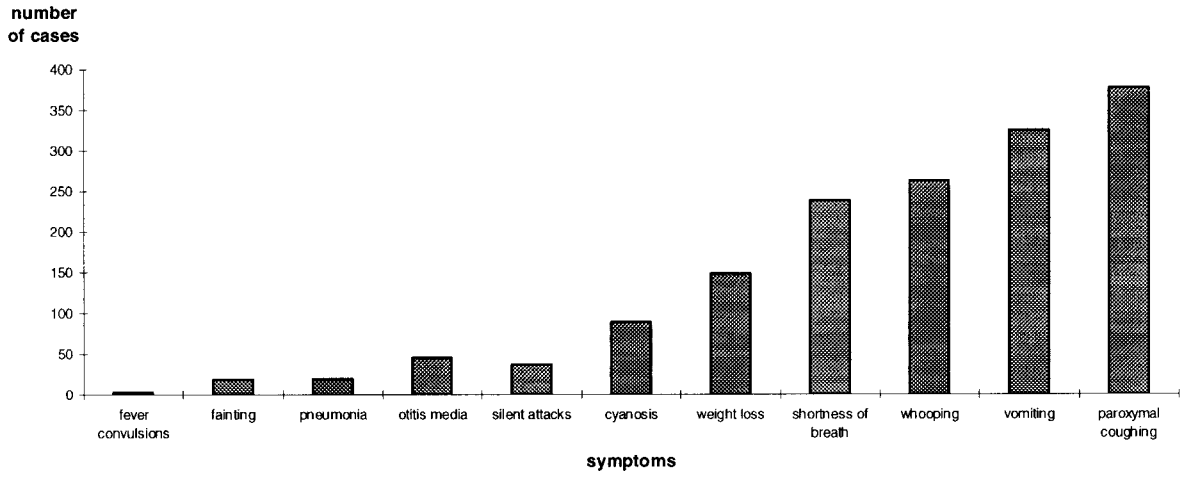

Figure 3.4.a Symptoms in notified pertussis cases (<16 years) (n=402)

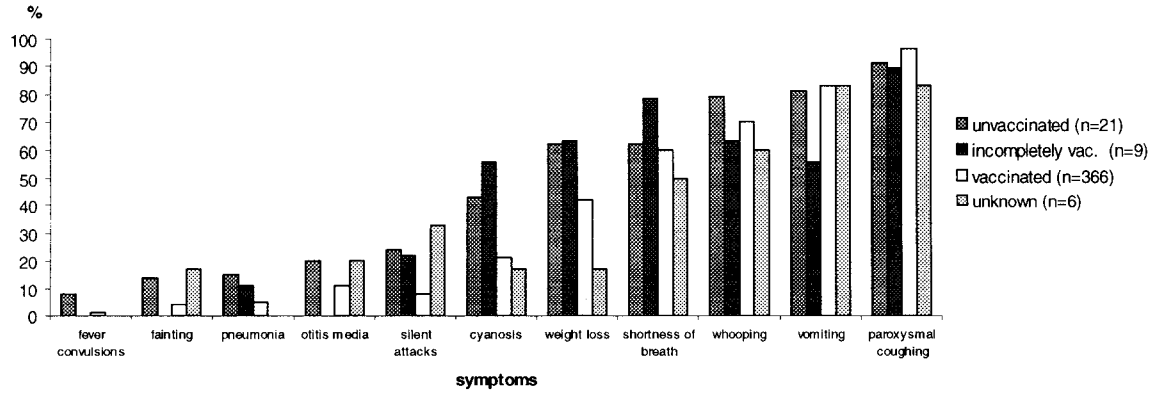

Figure 3.4.b Relative distribution of symptoms in each vaccination group in notified pertussis cases (<16 years) (n=402)

Figure 3.4.c shows some slight age effects within the vaccinated cases. With increasing age the frequency of reported fainting, otitis media, cyanosis, shortness of breath and whooping decreases. For other symptoms the differences between the age groups were not consistent e.g.: less paroxysmal cough and weight loss in the 7 to 11 months old children compared with the older age groups; less vomiting in the 10-15 year old children compared with the younger age groups.

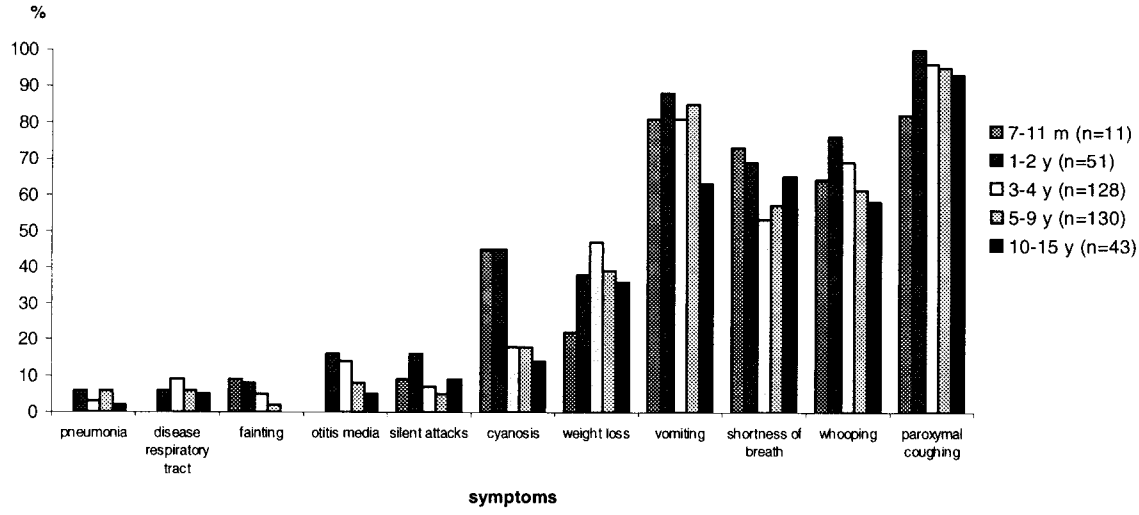

Figure 3.4.c *Relative distribution of symptoms in each age group in vaccinated notified pertussis cases (<16 years) (n=366)*

Of the notified cases 73% was still having symptoms at the moment of filling in the questionnaire (table 3.12). Most mentioned symptoms were coughing and paroxysmal coughing with or without other symptoms such as vomiting, shortness of breath, infection and having a cold.

Table 3.12 *Condition notified pertussis cases at the moment of filling in the questionnaire (after ≥ 6 weeks after onset of diseas) (<16 y)*

condition	unvaccinated n=21* (%)	incompletely vac. n=9* (%)	vaccinated n=366* (%)	unknown n=6* (%)	total n=402* (%)
symptoms at the moment					
yes	14 (67%)	7 (78%)	267 (73%)	4 (67%)	292(73%)
no	7 (33%)	2 (22%)	92 (25%)	2 (33%)	103(26%)
don't know	--	--	6 (2%)	--	6 (2%)
nature of symptoms					
paroxysmal coughing and other symptoms	6 (43%)	6 (86%)	140 (52%)	1 (1%)	153(52%)
only paroxysmal coughing	3 (21%)	1 (14%)	56 (21%)	--	60 (21%)
coughing only	5 (36%)	--	68 (26%)	3 (75%)	76 (26%)
other symptoms	--	--	27 (10%)	--	27 (9%)

* the true total number of cases varies due to excluded cases with missing values

In table 3.13 shows among others the number days the patient could not go to e.g. the nursery or school because of the illness. Forty-five percent of the cases did not stay home at all of which more vaccinated than unvaccinated. A few cases (7%) stayed home for at least 2 weeks. Some cases visited the family doctor more than 4 times (18%). Thirty-one percent consulted a specialist and in 21 cases hospital admission was needed; significantly more among unvaccinated than vaccinated (Fisher t-test: $p<0.05$). According to age, 7 hospitalised cases were less than 3 months of age; 4 cases were 3 to 11 months, 8 cases were 1 to 4 years and 2 cases were older than 4 years. Most cases took medication prescribed by the doctor (87%) including antibiotics (78%). Only 6 cases received preventive antibiotics in case others in his/her environment had pertussis as well. Cases who received antibiotics for preventive or therapeutic reason did not have less severe or frequent symptoms compared with those cases without antibiotics.

Table 3.13 Impact of pertussis on notified pertussis cases according to vaccination status and medication (<16 y)

impact of pertussis	unvaccinated n=21* (%)	incompletely vac. n=9* (%)	vaccinated n=366* (%)	unknown n=6* (%)	total n=402* (%)
absence					
no	6 (32)	3 (38)	163 (46)	3 (50)	175 (45)
1-3 days	6 (32)	1 (13)	80 (22)	3 (50)	90 (23)
4-7 days	2 (11)	--	55 (15)	--	57 (15)
8-14 days	1 (5)	1 (13)	35 (10)	--	37 (10)
> 14 days	3 (16)	3 (38)	22 (6)	--	28 (7)
still home	1 (5)	--	1 (0)	--	2 (0)
consults family doctor					
no	--	--	9 (2)	1 (17)	10 (3)
1-2 times	9 (43)	3 (33)	143 (40)	2 (33)	157 (39)
3-4 times	5 (24)	3 (33)	143 (40)	1 (17)	152 (38)
>4 times	4 (19)	3 (33)	63 (17)	2 (33)	72 (18)
don't know	3 (14)	--	4 (1)	--	7 (2)
consults specialist	13 (62)	6 (67)	101 (28)	3 (50)	123 (31)
hospital admission					
no	12 (57)	8 (89)	344 (94)	6 (100)	370 (92)
due to pertussis	4 (19)	1 (11)	8 (2)	--	13 (3)
due to pertussis and other cause	4 (19)	--	4 (1)	--	8 (2)
due to other cause	1 (5)	--	9 (2)	--	10 (2)
medication					
yes	18 (86%)	8 (100%)	315 (87%)	6 (100%)	347(87%)
no	3 (14%)	--	48 (13%)	--	51 (13%)
preventive antibiotics**	--	1 (20%)	5 (3%)	--	6 (3%)

* the true total number of cases varies due to excluded cases with missing values

** only if other pertussis cases were contacted

3.2.10 Symptoms, clinical course and disease impact in notified cases ≥ 16 years

Table 3.14 presents the frequencies of coughing or illness at the moment of filling in the questionnaire. Sixty percent of the cases were still coughing at the moment of filling in the questionnaire while 80% was not recovered also due to other symptoms. No significant differences were found between the vaccination groups. Table 3.15 shows that the median duration of coughing was 6 weeks in total to 9 weeks for those with symptoms at the moment of filling in the questionnaire. The median total duration of illness was 9 weeks in total and 11 weeks for those with still symptoms. The most frequent number of times of coughing was during the day (8). No significant differences were found between the vaccination groups.

Table 3.14 Frequency of coughing and illness at the moment of filling in the questionnaire (≥ 6 weeks after onset of disease) in notified cases according to vaccination status (≥ 16 y)

	unvaccinated n=12* (%)	incompletely vac n=3* (%)	vaccinated n=38* (%)	unknown n=52*(%)	total n=105* (%)
paroxysmal coughing	3 (30%)	2 (67%)	16 (46%)	17 (37%)	38 (40%)
paroxysmal coughing so far	7 (70%)	1 (33%)	19 (54%)	29 (63%)	56 (60%)
symptoms over ***	1 (9%)	--	8 (22%)	11 (22%)	20 (20%)
symptoms at the moment***	10 (91%)	3 (100%)	29 (78%)	39 (78%)	81 (80%)

* the true total number of cases varies due to excluded cases with missing values

** symptoms other than coughing

Table 3.15 Duration of coughing and illness, times of coughing and duration of coughing spell in notified cases according to vaccination status (≥ 6 weeks after onset of disease)(≥ 16 y)

duration and times (median (range))	unvaccinated n=12*	incompl. vac. n=3*	vaccinated n=38*	unknown n=52*	total n=105*
weeks paroxysmal coughing	6 (4-10)	10 (8-12)	5 (2-17)	8 (2-14)	6 (2-17)
weeks paroxysmal coughing so far	10 (6-11)	10	9 (6-16)	9 (5-25)	9 (5-25)
times paroxysmal coughing daily	7 (1-10)	8	6 (2-20)	8 (2-30)	8 (1-30)
times paroxysmal coughing night	4 (2-10)	8	5 (2-12)	5 (2-12)	5 (2-12)
minutes paroxysmal coughing	2 (1-30)	11 (2-20)	3 (1-15)	2 (1-15)	2 (1-30)
weeks symptoms total	8	--	11 (4-19)	9 (4-15)	9 (4-19)
weeks symptoms so far	10 (9-16)	18 (15-27)	10 (6-23)	11 (6-35)	11(6-35)

* the true total number of cases varies due to excluded cases with missing values

Most frequent symptoms among cases of 16 years and older were (paroxysmal) coughing, whooping, vomiting and shortness of breath (table 3.16). Symptoms such as cyanosis and fainting, mostly seen as a result of shortness of breath were less frequently reported among older cases compared with the younger age group (<16 years). No significant differences were found between the vaccination groups.

Table 3.16 Reported symptoms in notified pertussis cases according to vaccination status (≥ 16 y) *

symptoms	unvaccinated n=12* (%)	incompl. vac n=3* (%)	vaccinated n=38* (%)	unknown n=52* (%)	total n=105* (%)
coughing	11 (100)	3 (100)	38 (100)	52 (100)	104 (100)
paroxysmal coughing	10 (100)	3 (100)	36 (95)	45 (90)	94 (93)
whooping	9 (82)	2 (67)	30 (83)	38 (81)	79 (81)
vomiting	7 (70)	3 (100)	27 (71)	32 (63)	69 (68)
shortness of breath	8 (80)	2 (67)	27 (71)	34 (67)	71 (70)
cyanosis	1 (10)	--	4 (11)	5 (10)	10 (10)
fainting	1 (10)	--	4 (11)	9 (18)	14 (14)
fever	5 (45)	1 (33)	9 (24)	23 (44)	38 (37)
weight loss	5 (56)	1 (50)	8 (24)	16 (32)	30 (32)
complications					
pneumonia	--	--	--	2 (4)	2 (2)
disease respiratory tract	1 (9)	--	3 (8)	2 (4)	6 (6)
otitis media	--	--	--	1 (2)	1 (1)
bleeding eye	1 (9)	--	2 (5)	2 (4)	5 (5)
muscle pain ribs/shoulders	1 (9)	--	7 (18)	7 (14)	15 (15)
inguinal hernia	--	--	--	1 (2)	1 (1)
other complications	--	--	1 (3)	4 (8)	5 (5)
no complications	8 (73)	2 (67)	23 (61)	34 (67)	67 (65)
median max. temp. (range)	38.2(37.9-38.5)	38.9(38.9)	38.6 (38.6)	38.4(37.6-39)	38.5(37.6-39)
median weight loss (kg)(range)	1.3 (1-2)	3	2.5 (1.5-5)	3.5 (2-8)	3 (1-8)

* the true total number of cases varies due to excluded cases with missing values for some symptoms

Figure 3.5.a shows frequency of severe symptoms or complications among notified cases of 16 years and older as presented in table 3.18. In figure 3.5.b no clear differences could be observed in the frequency of symptoms between the vaccination groups except for more frequently weight loss among the unvaccinated and incompletelyly vaccinated cases.

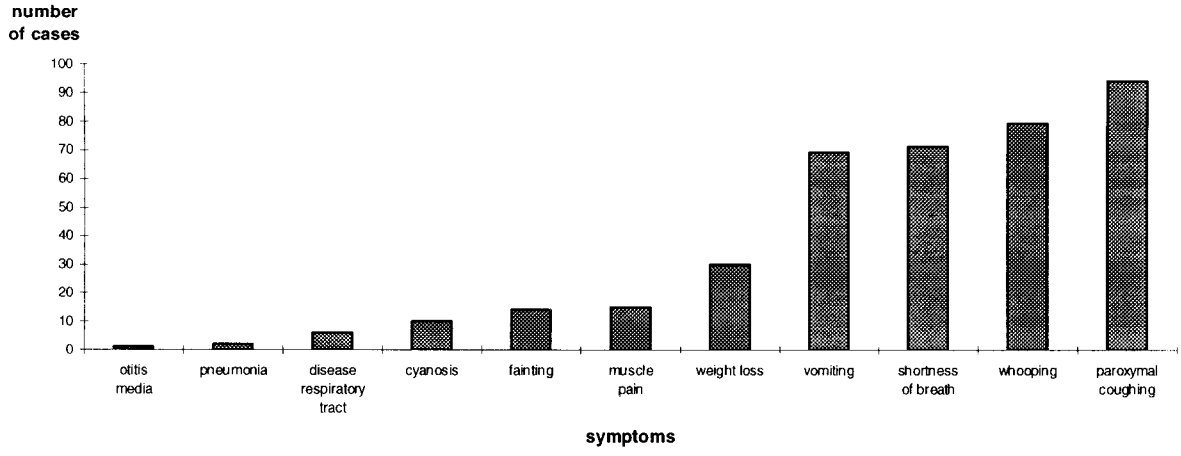

Figure 3.5.a Reported symptoms in notified pertussis cases (n=105)

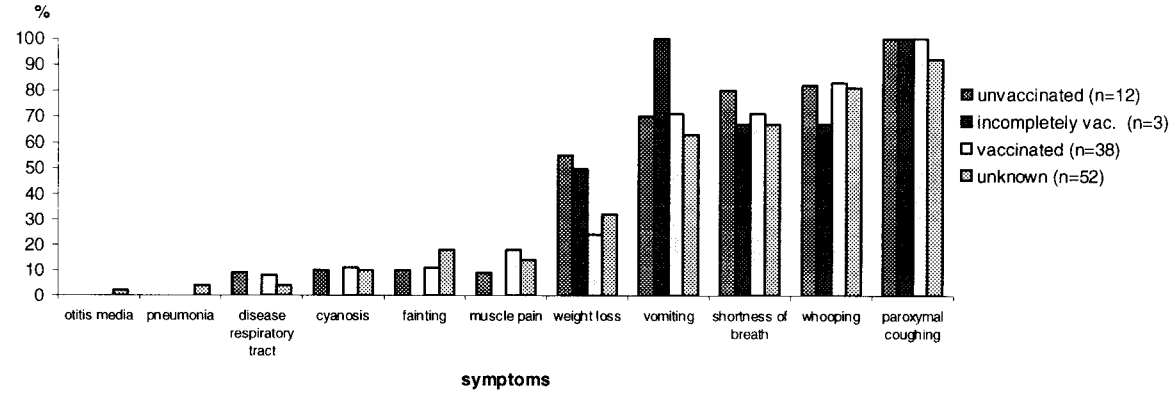

Figure 3.5.b Relative distribution of symptoms in each vaccination group in notified pertussis cases (n=105)

Within the vaccinated cases, no statistical significant differences were found between the age groups (figure 3.5.c). However, symptoms seemed to be less frequently reported in vaccinated cases aged 25-49 years compared with cases aged 16 to 24 years.

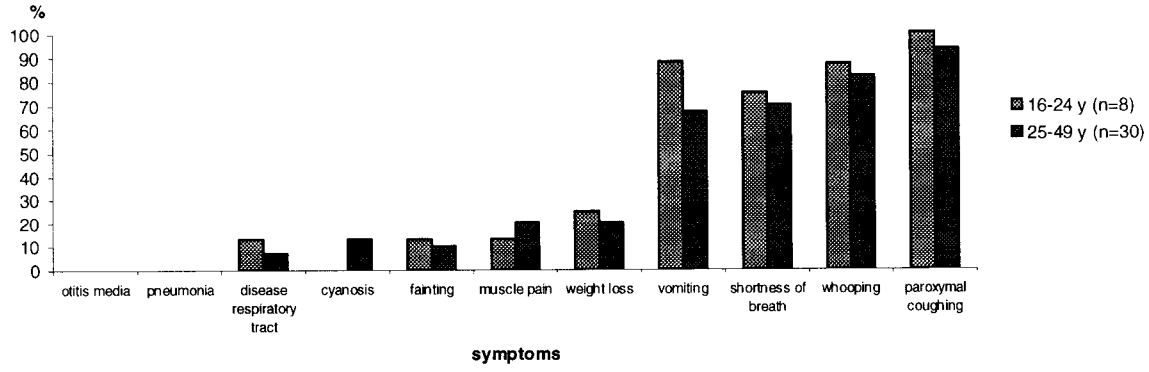

Figure 3.5.c *Relative distribution of symptoms in each age group in notified vaccinated pertussis cases (n=38)*

Table 3.17 shows that 77% of the older notified cases reported that they were not recovered from pertussis yet. In that case most of them were still coughing with symptoms such as vomiting, shortness of breath or having a cold.

Table 3.17 *Condition notified pertussis cases at moment of filling in questionnaire (≥ 6 weeks after onset of disease) (≥16 years)*

	unvaccinated n=12* (%)	incompletely vac. n=3* (%)	vaccinated n=38* (%)	unknown n=52* (%)	total n=105* (%)
symptoms at the moment					
yes	10 (91%)	3 (100%)	29 (76%)	39 (76%)	81 (79%)
no	1 (9%)	--	8 (21%)	11 (22%)	20 (19%)
don't know	1 (9%)	--	2 (5%)	1 (2%)	4 (4%)
nature of symptoms					
paroxysmal coughing and other symptoms	2 (22%)	--	7 (24%)	11 (21%)	20 (26%)
paroxysmal coughing only	--	2 (67%)	7 (24%)	5 (14%)	14 (18%)
coughing only	7 (78%)	--	9 (31%)	8 (23%)	24 (32%)
other symptoms	--	1 (33%)	6 (21%)	11 (31%)	18 (24%)

* the true total number of cases varies due to excluded cases with missing values

Most of the older notified cases did not stay at home because of the illness (58%) (table 3.18). However 10% reported that he or she stayed at home for at least 2 weeks. Many cases reported to have consulted a specialist (21%). In one case hospital admission was necessary due to pertussis. No significant differences were found between the vaccination groups. In 84% the physician prescribed the medication of which 73% antibiotics. Three cases used antibiotics for preventive reasons. Symptoms of cases who used antibiotics did not differ from those without antibiotics.

Table 3.18 Impact of pertussis on notified pertussis cases according to vaccination status and medication (≥16 years)

Impact of pertussis	unvaccinated n=12* (%)	incompletely vac. n=3* (%)	vaccinated n=38* (%)	unknown n=52* (%)	total n=105* (%)
absence					
no	9 (82)	1 (33)	21 (57)	28 (56)	59 (58)
1-3 days	--	1 (33)	5 (14)	8 (16)	14 (14)
4-7 days	--	--	3 (8)	3 (6)	6 (6)
8-14 days	--	1 (33)	2 (5)	3 (6)	6 (6)
> 14 days	2 (18)	--	5 (14)	3 (6)	10 (10)
still home	--	--	1 (3)	5 (10)	6 (6)
consults family doctor					
no	--	--	--	2 (4)	2 (2)
1-2 times	6 (55)	--	16 (42)	21 (40)	43 (41)
3-4 times	4 (36)	3 (100)	18 (47)	20 (38)	45 (43)
>4 times	1 (9)	--	4 (11)	8 (15)	13 (13)
don't know	--	--	--	1 (2)	1 (1)
consults specialist	4 (40)	2 (67)	6 (16)	10 (19)	22 (21)
hospital admission					
no	10 (100)	2 (67)	37 (97)	48 (98)	97 (97)
due to pertussis	--	--	--	1 (2)	1 (1)
due to something else	--	1 (33)	1 (3)	--	2 (2)
medication					
yes	10 (91%)	2 (67%)	33 (89%)	40 (80%)	85 (84%)
no	1 (9%)	1 (33%)	3 (8%)	9 (18%)	14 (14%)
preventive antibiotics**	--	--	1 (5%)	2 (7%)	3 (5%)

* the true total number of cases varies due to excluded cases with missing values

** only if other pertussis cases were contacted

3.2.11 Case definition

Figure 3.19 shows the number of cases, which met the criteria for notification for typical and atypical pertussis (appendix II). A few criteria could not be checked because they were not asked through the questionnaire: contact with confirmed pertussis case, local pertussis outbreak and leucocytosis. Still, 82% of the cases met the notification criteria for typical and 6% for atypical pertussis.

Table 3.19 Notified cases according to the case definition

criteria for diagnosis	notifications <16 y (n=402)	notifications ≥16 y (n=107)	total notifications (n=509)
typical pertussis	326 (81%)	92 (88%)	418 (82%)
atypical pertussis	29 (7%)	3 (3%)	32 (6%)
missing	47 (12%)	10 (10%)	57 (11%)

4. Validation vaccination status

4.1 Method

4.1.1 Verification vaccination status between the various sources

As described in paragraph 2.1.2. the physician or parental vaccination data were verified at two health centres and the Provincial Vaccination Administration with permission of the parents (written informed consent). The choice of health centre depended on the age of the patient. In general, the CB's keep the vaccination documents until the child is about 4 years of age. After this period, the documents are usually sent to the GGD's. For this reason, if the child was born after January 1993, the vaccination data were retrieved from the CB. Vaccination data of children born before January 1994 were obtained from the GGD's. Of children born in 1993, the vaccination status was collected of both centres. Of all patients younger than 16 years of age the PEA was asked for vaccination status information as well. The collected information included the number of pertussis vaccinations and the date (day/month/year) on which the vaccinations were administered. The date of the PEA included only the month and year of vaccination. Thus, depending on the age of the case the CB and/or a GGD was approached and in all cases younger than 16 years of age the PEA was approached as well.

For verification we compared the vaccination status recorded by the various agencies on type of vaccination. The information of the CB was used as the 'golden standard'. If no information was collected from the CB, the GGD was used as the 'golden standard'. In the NSCK study the vaccination status was classified according to information from the highest ranking source in the following hierarchy: CB, GGD, NSCK (paediatrician), PEA. For the notification study the following hierarchy was used: CB, GGD, vaccination certificate (parents), PEA. For analyses, vaccines administered after the first day of illness were not included to determine the vaccination status.

4.1.2 Verification vaccination status of the routine notification system

Data of notification study and the routine notification data of 1997 were linked to compare the verified vaccination status with the registered vaccination status data in the routine notification system. In general, the physician collected the vaccination status which is registered in the routine notification data.

4.2 Results

4.2.1 Sources used for the verification of the vaccination status

Table 4.1 shows the result of efforts done to verify the vaccination status. Because most of the NSCK cases were too young to be vaccinated (41%), no records of vaccination were available at any source. Of 21 children (11%) no informed consent was returned to verify the vaccination status. In 4% of the cases the verification at the agencies yielded no response. Of 79 cases the vaccination status could be retrieved. The final vaccination status was based (according to the hierarchical order) on records of the CB in 58% of the cases, on the GGD for 14%, on the physician's records for 19% and on the PEA for 9% of the cases.

In the notification study only 2% was too young to be vaccinated. Of 388 cases (97%) vaccination records were available at the various sources. For analyses, the vaccination status was in 26% based on the CB records, 42% on the GGD records, 30% on parental information (vaccination certificate) and in 3% on the PEA records.

Table 4.1 *Verification vaccination status according to information from highest ranking sources from which vaccination data were available in NSCK and notification study*

source	NSCK (n=180)		notification study (n=402)	
	n	(%)	n	(%)
too young to be vaccinated	73	(41%)	9	(2%)
no informed consents for verification	21	(12%)	2	(0.5%)
reason for not to be vaccinated		--	2	(0.5%)
no response from agencies	7	(4%)	1	(0.2%)
vaccination data available	79	(44%)	388	(97%)
vaccination data available*				
CB	46	(58%)	100	(26%)
GGD	11	(14%)	163	(42%)
paediatrician / parental information	15	(19%)	115	(30%)
PEA	7	(9%)	10	(3%)

* information from highest ranking sources in following hierarchy: CB, GGD, paediatrician/parental information and PEA

4.2.2 Response various sources

Table 4.2 and 4.3 show the response of the agencies. Information about the vaccination status in the NSCK was most frequently available at the paediatricians (89%). However, in case complete information was asked including the type and date of the administered vaccines, only 33% of the NSCK paediatricians had detailed information. The response and availability of information at the other agencies were comparable. In the notification study generally the obtained vaccination information from various sources was complete as well.

Table 4.2 *Vaccination status of pertussis cases (age >2 months) registered by various sources in NSCK (n=104)*

vaccination status	CB* n=80 (≤ 4 y) (%)	GGD** n=30 (≥ 4 y) (%)	physician/parents n=104 (%)	PEA n=104 (%)
response	44 (55%)	10 (33%)	93 (89%)	53 (51%)
complete information***	44 (55%)	10 (33%)	34 (33%)	53 (51%)

* information about vaccination status only retrieved at CB for cases born after January the first 1993

** information about vaccination status only retrieved at CB for cases born before January the first 1994

*** including type of vaccination and date administered

Table 4.3 *Vaccination status of pertussis cases (age >2 months) registered by various sources in notification study (n=402)*

vaccination status	CB* n=169 (≤ 4y) (%)	GGD** n=286(≥ 4 y) (%)	physician/parents n=393 (%)	PEA n=393 (%)
response	95 (56%)	173 (61%)	367 (93%)	322 (82%)
complete information***	92 (54%)	164 (57%)	347 (88%)	322 (82%)

* information about vaccination status only retrieved at CB for cases born after January the first 1993

** information about vaccination status only retrieved at CB for cases born before January the first 1994

*** including type of vaccination and date administered

4.2.3 Results verification of the various sources

Table 4.4 shows the number of incorrect data. Data of the paediatricians were not compared with the data obtained by the other sources because the information was not detailed enough. When the vaccination status retrieved from the various agencies was compared with each other, 7 times the vaccines were not equal: DT-IPV instead of DTP-IPV vaccine and vice versa. Six times (12%) the PEA reported an incorrect vaccination status compared with the CB in case both the information of the PEA and the CB was known (n=52). These differences were only found for those vaccines administered after the onset of disease. The PEA reported one time incorrectly compared with the GGD (n=12).

In the notification study, 22 times the vaccines were not equally reported by the various agencies (table 4.5). The information of the PEA was for 2 cases incorrectly reported compared with the information of the CB (n=92). The information of the vaccination certificate was for 2 cases incorrect compared with the CB's information (n=92). For 3 cases the vaccination certificate data was incorrect compared with the GGD's data (n=156). For five cases the PEA records were incorrect compared with the GGD (n=146). By comparing the data of the PEA with the vaccination certificate data (n= 291) it was not sure which source provided correct data. Probably the vaccination certificate data was for 2 cases incorrect because also CB information was available. Of the other 8 times the PEA data might be wrong but this remains unsure.

Table 4.4 Verification of vaccination status of NSCK study

sources	linked cases	number of cases with incorrect data	source with incorrect data
CB and PEA	52	6 (12%)	PEA
GGD and PEA	12	1 (8%)	PEA

Table 4.5 Verification of vaccination status of notification study

sources	linked cases	number of cases with incorrect data	source with incorrect data
CB and PEA	92	2 (2%)	PEA
CB and vaccination certificate	92	2 (2%)	vaccine certificate
GGD and vaccination certificate	156	3 (2%)	vaccine certificate
GGD and PEA	146	5 (3%)	PEA
vaccination certificate and PEA	291	10 (3%)	2 times vaccine certificate, 8 times PEA

4.2.4 Results verification vaccination status of the routine notification system

Table 4.6 and 4.7 show the result of linkage with the routine notification data according to the vaccination status. In 29 cases (6%) no linkage was possible with the notification data. Overall, the vaccination status data in the routine system was similar with the verified vaccination status data in the notification study except for a few cases. In the younger age group, seven cases were classified as vaccinated according to the routine data while the cases were 4 times unvaccinated and 3 times incompletely vaccinated according to the notification study (table 4.6). In the older age group, 3 cases were vaccinated according to the routine data but in the notification study the cases were reported as not vaccinated (2 cases) and incompletely vaccinated (1 case)(table 4.7). In 1 case the routine data reported incompletely vaccinated but according to the notification study he or she was vaccinated. Mainly in the older age group frequently no vaccination data were available and therefore classified as unknown however, in the routine notification system they were classified as unvaccinated (16 cases) or vaccinated (28 cases).

Table 4.6 *Verified vaccination status of cases in notification study compared with registered vaccination status of linked cases in the routine system (< 16 years) (n=381)*

routine notification / notification study	unvaccinated	incompletely vac.	vaccinated	unknown
unvaccinated	14	--	4	--
incompletely vaccinated	--	5	3	--
vaccinated	--	--	349	1
unknown	--	--	5	--

Table 4.7 *Verified vaccination status of cases in notification study compared with registered vaccination status of linked cases in the routine notification data (≥16 years) (n=97)*

routine notification / notification study	unvaccinated	incompletely vac.	vaccinated	unknown
unvaccinated	7	--	2	1
incompletely vaccinated	--	--	1	--
vaccinated	--	1	35	1
unknown	16	--	28	5

5. Discussion

5.1 Coverage of the paediatric surveillance

In the paediatric surveillance system 204 cases were reported. The number of hospital admissions below 15 years of age registered by the Foundation Information Centre of Health Care (SIG) was 480 in 1997. According to these numbers, the estimated coverage of the paediatric surveillance is 43%. The smaller number reported by the paediatric surveillance could partly be explained by a few missing cases due to non-participants among paediatricians. The overall non-response was 9% in the paediatric surveillance (17) and implies that some paediatricians did not report pertussis hospitalisations. On the other side, in the paediatric surveillance system, 9% of the patients was double reported due to cases transferred from one hospital to another and due to more than one admission. The SIG registered each hospital admission as a new case and this might increase the total number of hospitalisations. Another difference which might explain the large gap between the number of cases reported by the paediatric surveillance and the SIG is that the paediatric surveillance includes only those cases who consult the paediatrician while the SIG includes other specialists as well. Besides, the paediatric surveillance data covered cases with a hospital admission in 1997, whereas the SIG data included cases with a hospital discharge in 1997. Linkage was performed between the two data sources. About 25% of the paediatric surveillance cases could not be linked with the cases of the SIG. We have no reason to assume that the SIG wrongly registered hospitalisations for pertussis. Thus, the reason for no linkage is likely due to a lack of reliable variables from the SIG e.g. no date of birth but only age in months and years, no initials or no last name were available. Nevertheless, the paediatric surveillance probably gives a good picture of all hospital admissions since the duration of hospital admission, the gender distribution and the overall age distribution reported by the paediatric surveillance and the SIG were similar. Further simplifications of the questionnaire used in the paediatric surveillance could encourage the response among the paediatricians.

5.2 Coverage and case-definition of the notification study

The main aim of the notification study was to investigate the severity of pertussis among notified cases. Of 402 cases younger than 16 years of age and of 105 cases of 16 years and older, additional data were collected on the clinical course of pertussis and the vaccination status. In the period of October until the end of January with an onset of disease in 1997, approximately 1034 cases were notified according to the routine notification system. The notification study covered about 50% of all cases. This gap is due to several factors:
(1) five Municipal Health Services (GGD) did not participate (attributed approximately 4% of the total number of cases); (2) notified patients who were not invited to participate by the family doctor or Municipal health service; (3) non-response (62 persons: 10%) among notified cases due to e.g. foreigners who did not speak Dutch.

Our study has an important limitation. Since the pertussis cases were retrieved from notified cases, only patients who met the case-definition for notification (see appendix II) were studied. The case-definition includes both clinical and laboratory criteria. The clinical symptoms are a serious cough lasting more than 2 weeks or cough attacks or cough followed by vomiting in combination with at least one of the following symptoms/findings: apnoea, cyanosis, characteristic cough with whooping, subconjunctival bleeding, leucocytosis, or contact with a person with confirmed or suspected pertussis in the previous 3 weeks. Laboratory confirmation is defined as either positive culture of *B. pertussis* or *B. parapertussis* or positive two-point serology. Retrospectively we tried to evaluate if the reported symptoms and diagnosis of the participants met the case-definition. Most of the cases (82%) appeared to be correctly notified with respect to the clinical part of the case-definition for typical pertussis. Laboratory confirmation was mostly based on one-point serology which is the common practice although the case definition strictly includes only cases based on positive two-point serology. Those cases that did not meet the criteria according to our analyses (11%) were probably correctly notified, but we did not have enough information e.g., about a local outbreak, leucocytosis or contact with a confirmed case, to include them. Our study was therefore selected towards typical pertussis.

Besides selection of cases by the method of screening, the results could be biased by response according to vaccination status. For example, parents of notified cases who refuse vaccination for religious reasons could be less motivated to respond. In our study only 5% (less than 16 years of age) was not vaccinated and this corresponds with the vaccination coverage. The percentage of unvaccinated cases younger than 16 years of age in the routine notification system was 4% and comparable with our study. Thus, a selection bias towards vaccinated cases was probably small. Another bias could have been introduced by a higher response among notified cases in those with severe pertussis symptoms compared with those with less severe symptoms. However, only 10% refused to participate and thus the bias due to selective response was probably small as well.

5.3 Age, gender and vaccination status distribution

A comparison of the age distribution in the paediatric surveillance with the notified study showed that most hospitalisations occur among very young infants. About half of the hospitalised cases were less than 3 months of age and 73% were less than 1 year (median: 4 months, range 0-150 months). The age distribution differs from a French study in 1993-1994 (26) and an English study in 1995 (21) where 65% was less than 1 year and about 35% was less than 3 months of age. In contrast, Canadian and US data showed a proportion of about 90% of children less than 1 year (19, 20). Among the notified cases, 70% was younger than ten years, while the highest proportion was three to four years of age (26%). This age distribution with a peak at 4 years proves that immunity after vaccination wanes with time, which is in accordance with previous findings (12).

Gender was equally distributed among the hospitalised cases. Similar gender distributions were found in other studies (20,21,26) although the Canadian study found a higher proportion of hospitalised females (19). Among the notified cases younger than 16 years of age, gender was equally distributed (male: 49%, female: 51%) as well. The higher proportion of females cases as described in literature (22) could only be observed for notified cases of 16 years and older (32% male, 68% female). In the routine system we observed also a higher proportion of females (male: 37%, female: 63%) in the older age group. In literature this phenomenon is interpreted by the possibility of more contacts between women and children (23, 24).

As a consequence of a high vaccination coverage in the Netherlands (96%)(8), the vaccination status was strongly related with age. Of the hospitalised cases, 44% was unvaccinated which is lower compared with studies in France and the United States resp. 73% and 65%. Of the unvaccinated, 96% was younger than 3 months and too young to be vaccinated. Twelve percent was incompletely vaccinated of whom 95% 3-5 months of age. Thirty-one percent of the cases received 3 or 4 doses. For 14% of the cases the vaccination status was unknown. In the notification study only 7% were unvaccinated of whom 30% less than 3 months and 36% 16 years and older. Two percent of the cases was incompletely vaccinated and 80% was vaccinated. Of 11% of the notified cases the vaccination status was unknown but all of the cases were 16 years and older.

5.4 Laboratory diagnosis

The clinical diagnosis of *B. pertussis* infection was supported by a positive culture or PCR in 53% of the hospitalised cases and in only 4% of the notified cases. The high percentage of positive PCR and culture among hospitalisations is related with the opportunity to perform these diagnostics in an early stage of illness. The hospitalised cases are very young, often unvaccinated and symptoms are more severe and therefore earlier recognised compared with the notified cases. A validation study by Van der Zee et al. showed that the sensitivity of both culture and PCR decreased rapidly by the time the paroxysmal phase has developed (25). Baron et al. (26) found an odds ratio for positive culture of 2.9 when culture was done less then 15 days after the onset of disease compared with more than 15 days. Besides, the sensitivities of both PCR and culture were also found to be related with age of the patient. Van der Zee et al. (25) found that the sensitivity of the PCR in patients with <10 days of symptoms was 70%, 50% and 10% in the age group <1 year, 1-4 year, and ≥ 5 years, respectively. They found a low IgA response in the <1 year age group and suggested this might be related to the high number of samples positive in PCR and culture. Among the notified cases 15% was notified based on positive two-point serology and 39% on positive one-point serology. The case definition strictly includes only cases based on positive two-point serology, but in practice positive one-point serology is often applied for notification since pertussis is often confirmed on the basis of one sample (27).

More diagnostic information is preferable especially with respect to the serotype. A recent study in England-Wales indicated an increase of pertussis by serotype 1,2 and this serotype caused more severe symptoms (21). In addition, the association of the increased incidence of pertussis with the antigenic shifts in the *B. pertussis* population is very interesting and more detailed diagnostic information is preferable.

5.5 Clinical course in relation to vaccination status and age

5.5.1 Paediatric surveillance

A comparison of unvaccinated and vaccinated hospitalised children demonstrated that pertussis was more severe among unvaccinated infants. Unvaccinated young children had significantly more frequently episodes of cyanosis (77% vs. 40%) and apnoea (22% vs. 5%). Convulsions (3%), encephalopathy (1%) and atelectasis (1%) occurred only among the very young unvaccinated infants. Two male infants, three weeks of age, died due to pertussis. They had symptoms such as pneumonia, apnoea, respiratory insufficiency with artificial respiration, cyanosis and convulsions. In these infants no underlying disorders, preterm delivery and other infections were reported known to be risk factors for higher fatality rates (20,28). The percentage of children suffering from paroxysmal cough with whoops, fever, vomiting, collapse, pneumonia and respiratory insufficiency with artificial respiration did not differ significantly between vaccinated and unvaccinated children.

Overall, the children were hospitalised for a median duration of 8 days (range 0-44). Unvaccinated young infants were significantly longer hospitalised (12 days, range 1-44) compared to vaccinated children (5 days, 0-39). Patients were admitted after a median time of 14 days of illness, but for unvaccinated children the median time was 9 days (range 0-49) and differed significantly compared with vaccinated children (17 days, 3-199). The earlier and longer hospitalisation of very young infants with pertussis indicates severe disease although it is also related with a higher a priori probability for complications in this age group.

Since almost all unvaccinated children were less than 3 months while almost all vaccinated children were older, unfortunately we could not study in which extent the difference in severity was due to the difference in age. Buynder et al. found that unvaccinated patients were 1.5 times more likely to be admitted to hospital than vaccinated children (21). The decline of hospital admission in the period of 2 to 5 months of age would probably not be so strong without vaccination in this period. Within the unvaccinated children the severity was inversely related with age e.g. a higher frequency of encephalitis, convulsions, collapse, respiratory insufficiency, pneumonia, apnoea and cyanosis in infants younger than 1 month compared to those of 1 or 2 months of age, although the differences were not significant. Symptoms of unvaccinated cases more than 6 months of age did not differ statistically significantly with those in the younger age group but perhaps numbers are too small to detect differences. No consistent differences were found between the age groups within the vaccinated although the

young (3 months -2 years) suffered more frequently of cyanosis compared with the older age group (3-15 years). Pertussis vaccination has been shown to be efficacious in preventing severe disease after 3 doses (29). In our study no difference in severity was found between hospitalised cases that received 3 or 4 doses.

5.5.2 Notification younger than 16 years of age

When notified cases filled in the questionnaire too early, within the six weeks after the onset of disease, they were excluded (37 cases). The median duration between the onset of disease and the moment of filling in the questionnaire was 11 weeks. Still, it is possible that some symptoms or complications were missed because 79% of the cases were not recovered at the moment of filling in the questionnaire. However, we do not expect that the severity of symptoms or complications increase after such period of illness. No maximum period between the first day of illness and the moment of filling in the questionnaire was included in the criteria for exclusion. We assume that even after a long period, the specific symptoms such as whooping, cyanosis and breathing problems are still memorised by the participants. In general, we expect that the results are not strongly influenced by recall bias.

As many other studies, our study shows more frequent and severe symptoms among very young unvaccinated infants (5,9, 22,26). Unvaccinated children compared to vaccinated children developed more frequently cyanosis (43% vs. 21%), silent attacks (24% vs. 8%), fainting (14% vs. 4%), fever (57 % vs. 39%), weight loss (62% vs. 42%), pneumonia (15% vs. 5%) and ear infection (20 vs. 11%). However, only cyanosis and silent attacks differed significantly between the groups (Fisher t-test: $p<0.05$). Paroxysmal cough (96%), vomiting (82%), whooping (70%) and breathing problems (60%) were frequently reported but these symptoms did not differ significantly between the unvaccinated and vaccinated children. Overall, the duration of coughing and illness was long and varied widely. Most children had not recovered yet at the moment of filling in the questionnaire but the estimated mean period of illness is about 11 weeks. No significant differences of duration of coughing and illness were found between the unvaccinated and vaccinated group. Unvaccinated compared to vaccinated children consulted more often a specialist (62% vs. 28%) and were more frequently hospitalised (38% vs. 3%) (Fisher t-test: $p<0.05$). Unfortunately, it was not possible to study the effect of vaccination status on the severity of disease irrespective of age. Most children were vaccinated and only 12 older children were unvaccinated. Differences in symptoms among unvaccinated children with respect to age could not be observed. Within the vaccinated group a slight trend was noted between the different age groups where the young suffered more frequently of cyanosis, shortness of breath, fainting and otitis media. These differences, however, were not significant. A recent study in England-Wales showed that unvaccinated children are 1.82 times as likely as vaccinated children to exhibit complications after correcting for age (21). Similar results were found by Farizo indicating that clinical pertussis is less severe in vaccinated than in unvaccinated children of similar age with respect to longer coughing (>28 days), apnoea, pneumonia and seizures (9). In literature, population-based

studies of pertussis show widely different results in the frequency and severity of symptoms (1, 16,23) but results are difficult to compare due to differences in case finding, case-definition, age groups, vaccination history and the reliability of measurements. Due to the case-definition for notifications in The Netherlands, which include only cases with typical pertussis symptoms, we studied a selected population. Beforehand we expected that the clinical course in children vaccinated with the whole cell might be mitigated compared with classical pertussis. However, despite vaccination, children develop pertussis at a young age and we observed even the classical symptomatology of pertussis among notified vaccinated children.

5.5.3 Notifications of 16 years and older

Although adult pertussis is often unrecognised because of a different clinical and laboratory diagnosis (6, 33), we found almost similar reported clinical symptoms among notified adults compared with notified children. Off course, again the case-definition of our study selects only those adults with clinical pertussis. Overall, paroxysmal coughing (93%), whooping (81%), vomiting (68%) and shortness of breath (70%) were frequently reported among notified cases of 16 years and more. These frequencies of symptoms were similar compared with the younger age group. The number of cases with cyanosis (10%), pneumonia (2%) and otitis media (1%) were less frequently reported compared with the younger age group and other complications were less severe. The duration of coughing and illness and times of coughing showed a similar pattern compared with the younger age group. Because the immunity acquired by vaccination wanes after years we expected no differences between vaccinated and unvaccinated groups. This is consistent with our findings. More vomiting, whooping and paroxysms were found in female adults compared with male adults by Jenkinson (23) but could not be found in our study.

Complications due to pertussis in adults are less life threatening than in children, but transmission to the young infants may cause severe illness in the latter group (30, 31). Adults are often involved in the spread of pertussis (24). Deen et al. found in their household contact study that 53% of the index cases were 13 years and older (32). They also found that pertussis was laboratory confirmed in 46% of 114 exposed subjects without any clinical symptoms. To minimise the spread of pertussis, the diagnosis of pertussis in adults should be more often considered (33). In our study, 59% of the cases reported that their family members, classmates or colleagues etc. got pertussis as well. Brothers or sisters (27%) and classmates or colleagues (27%) were often reported to have pertussis as well. In the older age group, 48% reported their son or daughter had also pertussis symptoms. We do not know whether these were laboratory confirmed cases and whether they were index or secondary cases. To study the role of adults in the transmission of pertussis in the Netherlands a more detailed contact study is needed.

5.6 Medical Care

The severity of disease in those who received antibiotic prophylaxis before onset of disease did not differ from those without antibiotics but only 6 cases could be studied. The prescription of prophylaxis prior to disease onset is supposed to reduce the severity of disease and could be an important approach to prevent severe pertussis symptoms in the risk group (21). An extensive literature study by Dodhia (34) showed weak evidence to support the use of erythromycin within households preventing secondary cases of pertussis. The time between the onset of primary case and administering the antibiotics is an important factor and the effect is stronger in the early stage of disease. Antibiotics were also used as therapy, but the frequency and severity of symptoms did not differ compared with those without antibiotic treatments as expected according to literature (1). In addition, to study the effect of antibiotics we did not have information about the administered antibiotics.

5.7 Underlying disorders and risk factors

Among the hospital admissions a high incidence of COPD, asthma or chronic bronchitis was found: overall 29 cases (16%), 1% of the unvaccinated children and 34% vaccinated children reported one of these disorders. The difference between unvaccinated and vaccinated children can be easily explained by the age of unvaccinated which is too young for such disorders to be diagnosed. Twenty-one percent of the notified cases less than 16 years age reported these disorders, while 13% of notified cases of 16 years and more reported them. According to the Central Bureau for Statistics the prevalence of COPD, asthma and chronic bronchitis was 9.5% among children aged 0-14 years and 6.0-10.8% among cases of 15 years and older (8). Thus, the prevalence seems to be much higher among pertussis cases, both among the hospital admissions and notified cases although more specific age-related rates are needed. In literature a relation is described that pertussis vaccination can induce the risk on respiratory disorders (36). However, it is also known that individuals with respiratory disorders are more vulnerable for pertussis or show more severe symptoms.

Another risk factor for pertussis is preterm delivery and low birth weight. In a retrospective review of all deaths attributed to pertussis in 1992 and 1993 reported to the CDC, preterm delivery and young maternal age was found to increase the risk of death because of pertussis (5). Low birth weight children with reported pertussis were more likely to be hospitalised than normal birth weight children (35). In the paediatric study preterm delivery and low birth weight was not routinely asked. In the notification study for 5 cases younger than 1 year of age preterm delivery was reported (less than 38 weeks) with a median of 3 weeks. Numbers are too small to find any relation with the severity of pertussis.

5.9 Vaccine-efficacy

Previously we reported that during 1996 our routine notification data suggested a decrease in vaccine-efficacy (12). Overall, the vaccine-efficacy estimated by the screening method during 1996 was the lowest compared with previous years: 50.8% among 1-4 year old children, 31.1% 5-9 year old children while in 1989-1993 the vaccine-efficacy was about 90%. Vaccine efficacy based on surveillance data must be interpreted with caution due to possible biases (36,37). Biases such as (1) a change in selective reporting of vaccinated patients by physicians, (2) a change in missclassification of cases according to the vaccination status, (3) a change in vaccination coverage, (4) a higher propability of positive serological test due to priming in vaccinated persons were unlikely to explain the decrease in vaccine-efficacy completely. Furthermore, no indications were found of a decrease in vaccine quality or interference with other vaccines (12). However, vaccine-efficacy can be biased by the severity of disease. With the available surveillance data it was impossible to differentiate the vaccine-efficacy according to severity of disease. Vaccinated individuals are expected to have milder symptoms than unvaccinated individuals and also age is related with the severity of disease (1,21). Therefore we wanted to study the vaccine-efficacy stratified by age and severity of disease in a cases-control study. Unfortunately such a study was not feasible. Instead, we performed a study among hospitalised cases and notified cases as described above. However, due to criteria for notification, notified cases were a selected group with probably more severe pertussis. Furthermore, almost all unvaccinated cases were younger than 3 months and almost all vaccinated cases were older than one year. We could not differentiate between the effects of age and vaccination status. Despite these limitations we could conclude that among vaccinated children typical pertussis occurred. The complication rate was lower for vaccinated compared with unvaccinated cases.

We do not expect that the cases that occured before the epidemic were more severe than those notified in our study. This supports the finding of a decrease in vaccine-efficacy estimated previously by the screening method. We tried to estimate the vaccine-efficacy in different age-groups of cases of at least one year but many times this was not possible because of too low numbers of unvaccinated. However, the vaccine-efficacy estimated by the screening method for hospitalised cases was higher than for notified cases. This is an indication that the protection against severe disease is better than against less severe disease. The high number of vaccinated notified cases with typical pertussis symptoms and a long duration of disease show that the increase in pertussis incidence did not only result in mild disease.

5.10 Verification of the vaccination status

To minimise misclassification of the vaccination status, the information obtained from the physicians or parents was compared with records from the Child Health Centres, the Municipal Health Services and the Provincial Vaccination Administrations. The information of the Child Health Centres was considered to be the 'golden standard' because here the vaccines

are administered and directly registered in the child's record. We found that information from the various sources did not always correspond with each other. In particular, the information from the Provincial Vaccination Administration differed from the information from other sources. For example, if vaccination information was available both from the Administration and the Child Health Care (52 cases), the Administration reported 6 times (12%) that DTP-IPV vaccine was administered while the Child Health Centre reported the DT-IPV vaccine. These differences occurred only when the vaccines were administered after the onset of disease. Thus, interruption of the normal vaccination schedule because of pertussis, increases the chance of inaccurate registration by the Provincial Vaccination Administration. It was not possible to quantify the extent of inaccuracy in our study because in many cases no information was available from all the sources. However, it does support the findings of a small sized selective study in which children who were known to have received DT-IPV (proven by lot number) were found to be recorded as DTP-IPV recipients at the Provincial Vaccination Administration (personal communication: PE Vermeer-de Bondt). This demonstrates the need for a critical attitude if individual vaccination histories are obtained. Guided by the necessity to have detailed and valid information on vaccination history, e.g. for a controlled study on vaccine-efficacy, one should consider to obtain the information from more than one source. This implies that more efforts are needed to get the information because especially acquisition of information of the Child Health Centre is very time consuming.

Finally, the vaccination status was classified according to the information from the highest-ranking source in the following hierarchy: the Child Health Centre, the Municipal Health Services, the physician/parents and the Provincial Vaccination Administration. Because most of the hospitalised cases were too young to be vaccinated and because vaccination status was often based on records of the Child Health Centre (golden standard), we may safely assume that the chance of a missclassified vaccination status was small in the paediatric surveillance. For the notified cases we assume that the misclassification was also minimised because only for a few patients, the vaccination status was based on the information of the Provincial Vaccination Administration.

The vaccination status registered in the routine notification system was validated by using the verified vaccination status. In general, the vaccination status is registered correctly. In cases younger than 16 years of age, 7 (2%) were reported as vaccinated while the verified data implied unvaccinated or incompletely vaccinated. Estimations of vaccine-efficacy are based on proportion of vaccinated and incorrect reported vaccinated cases instead of unvaccinated might influence the vaccine-efficacy. When a misclassification of 2% is considered in the notification data of 1997, for example in the age group of 1-4 year old children, the vaccine-efficacy is increased but the trend of a low estimated vaccine-efficacy does not change.

6. General conclusions and recommendations

- Unvaccinated children were hospitalised more often than vaccinated children especially those children younger than 3 months of age. More severe symptoms and complications were observed in unvaccinated young children compared with vaccinated older children. Two infants, 3 weeks of age, died. Unvaccinated young children were hospitalised longer and sooner after the onset of disease. These findings show clearly that whooping cough remains a potentially severe and dangerous disease in unvaccinated young children.
- Typical classical pertussis symptoms is frequently observed in notified vaccinated children, but very severe illness with complications is unlikely. The impact of the disease is high. In general, the duration of illness was long, staying at home from school or work was often needed and many times medical services were contacted.
- Besides vaccination status, age is related with the severity of symptoms. Among unvaccinated children less than 3 months of age more severe disease was inversely related with age. Within vaccinated children, the young (5 months - 2 years) tended to have more frequently cyanosis, shortness of breath, fainting and otitis media than the older children (3-15 years).
- Both in the paediatric surveillance and in the notification study, underlying respiratory disorders were frequently reported.
- The clinical course among notified adults, vaccinated or not, is similar to symptoms among notified vaccinated children, although complications are less reported and less severe.
- Both in the paediatric surveillance and in the notification study pertussis was almost always laboratory confirmed. Confirmation of pertussis by culture was more likely in hospitalised children than in notified children. In the latter group most of the pertussis cases were confirmed by serology.
- Inaccurate reporting of the vaccination status seem to increase when the normal vaccination schedule was interrupted because of observed pertussis. Overall, the vaccination status reported in the routine notification system was correct.
- Paediatric surveillance gives good information about the clinical course, diagnostics and vaccination status of severe cases of pertussis. The coverage is not optimal but it a useful informative system besides other data.
- Nation-wide data about hospital admissions due to pertussis remain relevant to monitor the severity of pertussis. Besides, it is an important reference for estimating the coverage of the paediatric surveillance.

According to the results of the paediatric surveillance and the notification study we recommend:

- Continuation of the paediatric surveillance in order to collect information about the hospitalised cases in 1999, to compare results from year to year, monitor the effect of the vaccination at an earlier age (first vaccination at 2 months) which has been implemented in the Netherlands since January 1999. In addition, since november 1997 the whole cell vaccin has been changed in accordance to extra (international) activity criteria and evalution by, among others, the paediatric surveillance is needed.
- Reduction of the number of questions in the paediatric questionnaire to stimulate response among paediatricians. On the other hand, add questions about serotype to study the relation between serotype and severity of disease.
- Assessment of sources of infection in young vulnerable infants and obtain insight into the role of adults as reservoirs of infection.

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Appendix I List of participating Municipal Health Services

	GGD
1	Gezondheidsdienst Streekgewest Westelijk Noord-Brabant
2	GG&GD Amsterdam
3	GG&GD Utrecht
4	GGD Amstelland-De Meerlanden
5	GGD Arnhem/Dienst Welzijn en Volksgezondheid
6	GGD Brabant-Noordoost
7	GGD De Friese Wouden
8	GGD Delftland
9	GGD Den Haag
10	GGD Duin-en Bollenstreek
11	GGD Eindhoven
12	GGD Flevoland
13	GGD Gooi en Vechtstreek
14	GGD Kop van Noord-Holland
15	GGD Midden-Holland
16	GGD Midden-Kennemerland
17	GGD Midden-Limburg
18	GGD Nieuwe Waterweg Noord
19	GGD Noord-en Midden-Drenthe
20	GGD Noord-Friesland
21	GGD Noord-Kennemerland
22	GGD Noord-Limburg
23	GGD Noordwest-Veluwe
24	GGD Oostelijk Zuid-Limburg
25	GGD regio Achterhoek
26	GGD regio IJssel-Vecht
27	GGD regio Nijmegen
28	GGD Regio Stedendriehoek
29	GGD Rivierenland
30	GGD Rotterdam e.o.
31	GGD Stad en Ommelanden /GGD Oost-Groningen
32	GGD Stadsgewest `s Hertogenbosch/ GGD Midden-Brabant
33	GGD Stadsgewest Breda
34	GGD Twente
35	GGD Waterland /GGD Zaanstreek
36	GGD West-Friesland
37	GGD West-Holland

38	GGD Westelijke Mijnstreek
39	GGD Zuid-Holland
40	GGD Zuid-Kennemerland
41	GGD Zuidelijk Zuid-Limburg
42	GGD Zuidhollandse Eilanden
43	GGD Zuidoost-Brabant
44	GGD Zuidoost-Drenthe
45	GGD Zuidwest-Drenthe
46	GGD Zuidwest-Friesland

Appendix II Case-definition for notification pertussis

1. **Pertussis**
The diagnosis is made on the following criteria:

1.1 Anamnestic one or more of the following symptoms:
a. A serious cough, with a duration of more than two weeks
b. Coughing attacks
c. Cough followed by vomiting

in combination with:

1.2 One or more of the following signs, symptoms or findings:
a. For young infants a period of apnoea and cyanosis after long-term coughing
b. For pertussis characteric cough with whooping
c. Subconjunctival bleeding
d. Contact with a individual suspected for pertussis or with a confirmed case with pertussis in the previous three weeks
e. The occurence of a pertussis outbreak locally
f. Leucocytosis from ≥ 15.000 lymphocytes per ml

and in combination with:

1.3 Positive bacteriological and/or serological findings in the patient, or in the index patient (epidemiological criteria (included in the case-definition in 1992).

NB *For serodiagnosis of pertussis the results are positive when a significant rise in titres in paired sera occured (positive two-point serology).*

2. **Atypical pertussis**
The diagnosis pertussis is made, when the patient coughs and the criteria described in 1.1 and 1.2 were not met, but the criteria in 1.3 were met.

NB *An individual without symptoms has not to be notified independently on microbiological or serological findings which indicate that the individual has a pertussis infection.*

Appendix III Questionnaire Paediatric surveillance

Naar aanleiding van uw melding aan het Nederlands Signalerings-Centrum Kindergeneeskunde van ziekenhuisopname van een patiënt met kinkhoest, verzoeken wij u deze vragenlijst zo volledig mogelijk in te vullen.

Bij vragen kunt u contact opnemen met de onderzoeker Dr.M.A.E.Conyn-van Spaendonck, Centrum voor Infectieziekten Epidemiologie, RIVM (telefoon 030-274 30 18). Hartelijk dank voor uw medewerking.

Naam signalerende kinderarts: .....

Naam ziekenhuis: .....

NSCK-code | K |

PERSOONSGEGEVENS VAN HET KIND MET KINKHOEST

1 Eerste letter voornaam _

2 Eerste letter achternaam _

3 Geboortedatum ☐☐-☐☐-19☐☐ (dag-maand-jaar)

4 Geboren na zwangerschapsduur van ☐☐ weken ☐ onbekend

5 Geboortegewicht ☐☐☐☐ gram ☐ onbekend

6 Geslacht ☐ jongen ☐ meisje

7 Woonplaats .....

8 Postcode ☐☐☐☐ ☐☐

ZIEKTEGEGEVENS

9 Eerste ziektedag (catarre of hoesten): ☐☐-☐☐-19☐☐ (dag-maand-jaar)

10 Klinische verschijnselen bij en/of tijdens opname (meer antwoorden mogelijk)

☐ koorts;

hoogst gemeten temperatuur ☐☐,☐ °C

☐ hoesten

duur: ☐☐ weken, vóór opname

aard: ☐ aspecifiek

☐ paroxysmaal (kinken)

☐ piepende inspiratie

☐ cyanose na hoestbui

☐ braken na hoestbui

☐ veel slijm rond mond, bellen blazen
☐ apneu / stille aanval
☐ collaps na hoestbui
☐ convulsies
☐ (broncho)pneumonie
☐ encephalopathie
☐ anders, namelijk . . . . . .

11 Heeft de patiënt tijdens opname zuurstof toegediend gekregen? ☐ ja ☐ nee

12 Is de patiënt tijdens opname kunstmatig beademd? ☐ ja ☐ nee

13 Is er sprake van een onderliggende respiratoire aandoening? ☐ nee
☐ ja, namelijk . . . . . .

14 Datum opname: ☐☐-☐☐-19☐☐ (dag-maand-jaar)

15 Datum ontslag: ☐☐-☐☐-19☐☐ (dag-maand-jaar)

16 Toestand bij ontslag: ☐ hersteld zonder restverschijnselen
☐ restverschijnselen:
☐ hoesten anders, namelijk . . . .
☐ overleden

VACCINATIE

17 Is patiënt gevaccineerd tegen kinkhoest? ☐ ja ☐ nee ☐ onbekend

18 Zo nee, wat is hiervan de reden? ☐ te jong voor vaccinatie
anders, namelijk . . . .

19 Zo ja, op welke data is gevaccineerd?

	dag	maand	jaar
1e	☐☐	-☐☐	-19☐☐
2e	☐☐	-☐☐	-19☐☐
3e	☐☐	-☐☐	-19☐☐
4e	☐☐	-☐☐	-19☐☐

20 Geven de ouders toestemming om gegevens over vaccinaties bij de entadministratie na te vragen? (dit is niet nodig bij kinderen jonger dan 3 maanden)

Zie bijgaande modelverklaring. ☐ ja ☐ nee ☐ onbekend

21 Indien ja, wordt een toestemmingsverklaring met deze vragenlijst meegestuurd? ☐ ja ☐ nee

DIAGNOSTISCHE GEGEVENS

22 Is er gekweekt? ☐ ja ☐ nee ☐ onbekend

23 Zo ja, resultaat kweek:

☐ negatief

☐ positief: verwekker . . . . . .

in . . . . . (materiaal)

24 Is serologisch onderzoek verricht? ☐ ja ☐ nee ☐ onbekend

25 Uitslag serologie:

☐ geen aanwijzing voor kinkhoest

☐ bewezen: seroconversie of significante titerstijging bij onderzoek van twee sera

☐ zeer suspect: hoge titer in één serum

☐ (nog) onbekend

26 Is er PCR onderzoek verricht? ☐ ja ☐ nee ☐ onbekend

27 Uitslag PCR:

☐ positief

☐ negatief

☐ onbekend

28 Is aangifte gedaan bij de Inspectie voor de Gezondheidszorg / GGD? ☐ ja ☐ nee ☐ onbekend

Verdere bijzonderheden of opmerkingen:

Graag zouden we een copie van de ontslagbrief van u ontvangen.

Gaarne per ommegaande retourneren in bijgesloten antwoordenvelop of naar RIVM, Centrum voor Infectieziekten Epidemiologie (pb.75), t.a.v. Dr.M.A.E.Conyn-van Spaendonck, Antwoordnummer 3205, 3720 FB BILTHOVEN

Appendix IV Informed consent Paediatric surveillance

NSCK

Nederlands Signalerings-Centrum Kindergeneeskunde

secretariaat: TNO-PG
Postbus 2215
2301 CE Leiden

TOESTEMMINGSVERKLARING KINKHOESTONDERZOEK

In Nederland worden alle kinderen op vrijwillige basis gevaccineerd tegen een aantal kinderziekten waaronder kinkhoest. Hierdoor komt deze ziekte sinds de jaren 50 veel minder vaak voor. Toch is het niet mogelijk alle gevallen van kinkhoest te voorkómen. Ook bij gevaccineerden kan de ziekte soms toch nog optreden, al is de kans veel kleiner dan voor niet-gevaccineerden.
Recent is er een overwachte toename van kinkhoest vastgesteld. Het is van groot belang te onderzoeken wat hiervan de oorzaak is, zodat eventueel maatregelen kunnen worden getroffen. Daarom worden door het Rijksinstituut voor Volksgezondheid en Milieu zo compleet mogelijke gegevens over ziektegevallen verzameld. Het gaat daarbij om informatie over ziekteverschijnselen, inentingen en laboratorium-onderzoek. Daarom willen wij uw toestemming vragen om van de gebruikelijke anonimiteit af te kunnen wijken en de naam van uw kind gebruiken bij de gegevensverzameling van dit onderzoek.

De ouders van

.....(voornaam)

.....(achternaam)

.....(geboortedatum, dag-maand-jaar)

.....(straat en huisnummer)

.....(postcode en woonplaats)

geven toestemming dat deze persoonsgegevens worden doorgegeven aan het Rijksinstituut voor Volksgezondheid en Milieu (RIVM). Deze gegevens zullen worden gebruikt om -indien van toepassing- exacte gegevens over de toegediende vaccins en uitslagen van laboratoriumonderzoek na te vragen. Het RIVM is gehouden aan een privacyreglement en draagt zorg dat de gegevens niet toegankelijk zijn voor derden.

.....(plaat, datum)

.....(handtekening van ouder)

.....(behandelend kinderarts)

.....(ziekenhuis, plaats)

Deze toestemming kunt u samen met de vragelijst sturen naar het RIVM, Centrum voor Infectieziekten Epidemiologie (Pb 75), t.a.v. M.A.E. Conyn-van Spaendonck, antwoordnummer 3205, 3720 FB BILTHOVEN.

Appendix V Vaccination form

GEGEVENS VACCINATIESTATUS 'AANGIFTE-PLUS'

NAAM INSTANTIE:

VACCINATIEGEGEVENS VAN:

Naam: Geb.datum:

Straat: Postcode en woonplaats:

Provincie: Codenummer: Geslacht:

Plaats en straat laatste vaccinatie:

AANKRUISEN WAT VAN TOEPASSING IS : **DKTP** → difterie, **kinkhoest**, tetanus en polio
DTP → difterie, tetanus en polio

	Soort inenting			Datum van inenting	Partij-/lotnr
1e.	❒ DKTP of ❒ DTP	of	❒ onbekend	|__|__| -- |__|__| -- |1|9|__|__| (dag maand jaar)	|__|__|__|__|__|
2e.	❒ DKTP of ❒ DTP	of	❒ onbekend	|__|__| -- |__|__| -- |1|9|__|__| (dag maand jaar)	|__|__|__|__|__|
3e.	❒ DKTP of ❒ DTP	of	❒ onbekend	|__|__| -- |__|__| -- |1|9|__|__| (dag maand jaar)	|__|__|__|__|__|
4e.	❒ DKTP of ❒ DTP	of	❒ onbekend	|__|__| -- |__|__| -- |1|9|__|__| (dag maand jaar)	|__|__|__|__|__|
5e.	.....	of	❒ onbekend	|__|__| -- |__|__| -- |1|9|__|__| (dag maand jaar)	|__|__|__|__|__|
6e.	.....	of	❒ onbekend	|__|__| -- |__|__| -- |1|9|__|__| (dag maand jaar)	|__|__|__|__|__|

Eventueel (indien gegevens niet aanwezig zijn) adres van consultatiebureau of waar anders voor het laatst gevaccineerd is:

Naam van vaccinerende instantie:.....

Adres:.....

Postcode:.....Plaats:.....

OPMERKINGEN:.....

Wilt u dit formulier retourneren naar: RIVM, Afdeling CIE, postbak 75, t.a.v. S.E. Neppelenbroek, Antwoordnummer 3205, 3720 VB Bilthoven. **Hartelijk bedankt !**

Appendix VI Matching Paediatric surveillance data - national hospital admission data

The NSCK cases were individually matched with the data of the SIG. For the SIG only age, gender, place of residence, date of hospital admission and date of discharge was available. Besides the NSCK cases in 1997 were reported by day of hospital admission while the SIG data in 1997 is based on the hospital discharges in 1997.
The matching was performed in the following steps:

1. matching gender, date of hospital admission, date of hospital discharge, age (months/years) and, first four characters of place of residence. Result: 41 matches
2. matching gender, date of hospital admission, date of hospital discharge and, first four characters of place of residence. Only matches included when age (months/years) was almost similar. Result:27 matches.
3. matching gender, date of hospital admission, date of hospital discharge and, age (months/ years. Only matches included when place of residence was plausible. Result: 23 matches.
4. matching gender, date of hospital admission and date of hospital discharge. Only matches included when age (months/years) and place of residence was almost similar. Result: 20.
5. matching gender, date of hospital admission, first four characters of place of residence and age (years/months). Result: 5 matches.
6. matching gender, date of hospital discharge, first four characters of place of residence and age (months/years). Result: 2 matches.
7. matching gender, date of hospital admission and, first four characters of place of residence. Only matches included when age (months/years) was almost similar. Result: 6 matches.
8. matching gender, date of hospital discharge and, first four characters of place of residence. Only matches included when age (months/years) was almost similar. Result: 4 matches.
9. matching gender, date of hospital admission and, age (months/years). Only matches included when place of residence was plausible. Result: 1 match.
10. matching gender, date of hospital discharge and, age (months/years). Only matches included when place of residence was plausible. Result: 2 matches.
11. matching, date of hospital admission, date of hospital discharge and, first four characters of place of residence. Only matches included when gender in SIG or NSCK was missing. Result: 1 match.
12. matching, date of hospital admission, date of hospital discharge and, age (years/months). Only matches included when gender in SIG or NSCK was missing. Result: 0 matches.

Records that were matches twice were excluded. In total 132 matches of which 2 did not meet the criteria (see paragraph 2.1.1.).

Appendix VII Method of laboratory Paediatric surveillance

Table Method of laboratory in pertussis NSCK cases

Method of laboratory	Number n	n=180 %
culture, serology and PCR	15	100
culture pos, serology no indication, pcr pos	3	20
culture pos, serology unknown, pcr pos	1	7
culture neg, serology no indication, pcr pos	6	40
culture neg, serology unknown, pcr pos	3	20
culture other, serology suspect, pcr pos	2	13
culture and serology	65	100
culture pos, serology proved	7	11
culture pos, serology suspect	4	6
culture pos, serology no indication	9	14
culture pos, serology missing	8	12
culture neg, serology proved	11	17
culture neg, serology suspect	14	22
culture neg, serology no indication	1	2
culture other, serology proved	6	9
culture other, serology suspect	1	2
culture unknown, serology proved	3	5
culture unknown, serology unknown	1	2
culture and PCR	10	100
culture pos, pcr pos	6	60
culture pos or other, pcr pos	2	20
culture neg, pcr pos	2	20
serology and PCR	10	100
serology suspect, pcr pos	2	20
serology no indication, pcr pos	1	10
serology unknown, pcr pos	4	40
serology suspect, pcr neg	3	30
culture	30	100
pos	30	100
serology	42	100
proved	21	50
suspect	19	45
unknown	2	5
PCR	5	100
pos	5	100
diagnostics unknown	3	100

Appendix VIII Informed consent Notification study

A	

Toestemmingsverklaring deelname aan landelijk onderzoek betreffende kinkhoest

Ondergetekende

- verklaart dat hij/zij een brief ontvangen heeft met informatie over het kinkhoest-onderzoek en van deze informatie kennis genomen heeft;
- heeft gelegenheid gekregen hierover iedere gewenste vraag te stellen;
- geeft toestemming aan het Rijksinstituut voor Volksgezondheid en Milieu (RIVM) om vaccinatiegegevens van zijn/ haar kind bij de Provinciale Entadministratie of Consultatiebureau op te vragen voor de in de informatiebrief beschreven doeleinden;
- weet dat de gegevens uit de vragenlijst en de vaccinatiegegevens van de Provinciale Entadministratie of Consultatiebureau vertrouwelijk worden verwerkt;
- is ervan op de hoogte dat bij vragen en contact kan worden opgenomen met de contactpersoon van de GGD.

Plaats.....Datum.....

Ouder(s)/verzorger(s) van:.....
(achternaam en voorletters van kind)

Handtekening ouder(s)/ verzorger(s):.....

Appendix IX Questionnaire Notification study (<16 years)

A	

VRAGENLIJST
VOOR DE OUDERS VAN KINDEREN MET KINKHOEST

Toelichting bij de vragenlijst

Deze vragenlijst bestaat uit 35 vragen. Het invullen van de vragenlijst duurt ongeveer 20 minuten. De vragen in de vragenlijst hebben betrekking op uw kind wat kinkhoest heeft gekregen. Omdat uw kind waarschijnlijk te jong zal zijn om de vragenlijst in te vullen, zijn de vragen gericht aan de ouder(s)/verzorger(s). Hierbij is het belangrijk antwoorden in te vullen die voor uw kind met kinkhoest gelden.

De vragenlijst begint met enkele algemene gegevens van uw kind met kinkhoest. Vervolgens worden vragen gesteld over de gezondheid van uw kind en welke klachten uw kind had door de kinkhoest. Tot slot worden enkele vragen gesteld over de inentingen die uw kind heeft gehad. Deze laatste gegevens over de inenting kunt u het beste uit het vaccinatieboekje of vaccinatiekaart halen.

Bij de meeste vragen staan meerdere antwoordmogelijkheden. Wilt u het antwoord aankruisen dat voor uw kind van toepassing is òf het beste bij de situatie van uw kind past? Bij een aantal vragen is er ruimte waar u zelf een antwoord in kunt vullen.

Bij sommige vragen wordt gevraagd naar een datum (bijvoorbeeld wanneer bij uw kind de klachten begonnen). Wij kunnen ons voorstellen dat u de **exacte** datum niet meer weet. Misschien kunt u in dat geval met behulp van een kalender of agenda toch een geschatte datum invullen. Op de nummertjes bij de antwoorden hoeft u niet te letten, deze dienen alleen voor onze verwerking.

Voorbeeld

Stel bijvoorbeeld dat de vragenlijst gaat over een jongetje, geboren 24-03-91. De ouder/verzorger van het jongetje vult de vragenlijst in met de gegevens over haar zoon. Dan ziet het voorbeeld er als volgt uit:

Wat is het geslacht van uw kind?

1 ■ jongen
2 ❒ meisje

Wat is de geboortedatum van uw kind?

|2|4| -- |0|3| --|1|9|9|1|

dag maand jaar

Dit geldt voor het invullen van alle vragen in de vragenlijst.
Wilt u bij **alle** vragen (tenzij anders vermeld) en antwoord aankruisen?

Veel succes bij het invullen van de vragenlijst!

ALGEMEEN

Hieronder worden enkele algemene vragen gesteld over de persoonsgegevens van uw kind en over het huishouden waar uw kind deel van uitmaakt.

1. Wie vult deze vragenlijst in?

1 ❒ ouder(s)/ verzorger(s) van kinkhoest-patiënt
2 ❒ iemand anders, namelijk:
.....
(invullen bijvoorbeeld zus of broer)

2. Wanneer vult u deze vragenlijst in?

|_|_| -- |_|_| --|1|9|_|_|
dag maand jaar

3. Wat is het geslacht van uw kind?

1 ❒ jongen
2 ❒ meisje

4. Wat is de geboortedatum van uw kind?

|_|_| -- |_|_| --|1|9|_|_|
dag maand jaar

5a. Uit hoeveel personen bestaat het huishouden waarvan uw kind deel uit maakt (inclusief uw kind)?

|_|_| personen

b. Met welke personen woont uw kind momenteel samen? *(meer antwoorden mogelijk)*

1 ❒ met zijn/haar ouder(s)/verzorger(s)
1 ❒ met kind of kinderen tot 4 jaar
1 ❒ met kind of kinderen van 4 tot 10 jaar
1 ❒ met kind of kinderen van 10 jaar en ouder

6. Bezocht uw kind in de periode dat hij/zij kinkhoest kreeg een crèche/kinderdagverblijf/peuterspeelzaal?

1 ❒ ja
2 ❒ nee

GEZONDHEID EN ZIEKTEGEGEVENS

Dit onderdeel van de vragenlijst bevat vragen over de gezondheid van uw kind en doorgemaakte ziekten **in de periode vóórdat uw kind kinkhoest kreeg.**

⇨ ***Wanneer uw kind ouder is dan 1 jaar, ga dan door naar vraag 9***

7a. Is uw kind te vroeg geboren?
(dus zwangerschapsduur is korter dan 40 weken)

1 ❒ ja
2 ❒ nee
3 ❒ weet ik niet

b. Zo ja, hoeveel weken te vroeg? |__|__| weken te vroeg

8. Wat was het geboortegewicht van uw kind?

1 |__|__|__|__| gram
2 ❒ weet ik niet

9. Wat was het gewicht van uw kind voordat hij/zij kinkhoest kreeg?

1 |__|__| kg
2 ❒ weet ik niet

10. Wat was de lengte van uw kind voordat hij/zij kinkhoest kreeg?

1 |__|, |__|__| meter
2 ❒ weet ik niet

11. Had uw kind reeds een ziekte of aandoening, **vóórdat** hij/zij kinkhoest kreeg?
(*meer antwoorden mogelijk*)

1 ❒ Astma, chronische bronchitis of COPD

1 ❒ Andere longziekte, namelijk.....

1 ❒ Ontsteking van de neusbijholte, voorhoofdsholte of kaakholte

1 ❒ Allergie, met allergische reacties van de luchtwegen bijvoorbeeld door hooikoorts en huisstofmijt

1 ❒ Allergie, met allergische reacties van de huid bijvoorbeeld door contacteczeem

1 ❒ Allergie, met allergische reacties veroorzaakt door bepaalde voedingsmiddelen bijvoorbeeld koemelkeiwit

1 ❒ Ziekte van zenuwstelsel (bijvoorbeeld epilepsie), namelijk.....

1 ❒ (Koorts-)stuipen

1 ❒ Complicaties na te vroeg geboren, namelijk.....

1 ❒ Ontwikkelingsstoornis, namelijk.....

1 ❒ Andere ziekten of aandoeningen namelijk.....

1 ❒ Geen ziekten of aandoeningen

12a. Heeft uw kind eerder kinkhoest gehad? 1 ❒ ja
2 ❒ nee

b.Zo ja, wanneer? |1|9| | | jaar

13a. Zijn er andere personen in uw omgeving die kinkhoest hebben gekregen in de periode van **6 weken vóór** tot **6 weken ná** de eerste ziektedag van uw kind?

1 ❒ ja
2 ❒ nee, ⇨ *ga verder naar vraag 14*

b. Zo ja, welke personen waren dat, wanneer, op **welke leeftijd** en **waar** in de omgeving?
Voorbeeld 1: uw buurjongen van 8 jaar had kinkhoest 4 weken voordat uw kind kinkhoest kreeg.
Voorbeeld 2: het broertje van 6 maanden kreeg kinkhoest 3 weken nadat uw andere kind kinkhoest kreeg. Indien meer dan 4 personen in uw omgeving kinkhoest hebben (gehad) vult u dan **alleen** het aantal personen in onderin de tabel.

	Persoon in omgeving	Leeftijd van die persoon	Waar in de omgeving	Tijdsduur **vóór** of **na** het moment dat uw kind kinkhoest kreeg
Voorbeeld 1	*buurjongen*	*8 jaar/~~maanden~~*	*buurt*	*4 weken voor /~~na~~*
Voorbeeld 2	*broertje*	*6 ~~jaar~~/maanden*	*gezin*	*3 weken ~~voor~~ /na*
Persoon 1:	.....	..... jaar/maanden	.....	.... weken voor / na
Persoon 2:	.....	..... jaar/maanden	.....	.... weken voor / na
Persoon 3:	.....	..... jaar/maanden	.....	.... weken voor / na
Persoon 4:	.....	.... jaar/maanden	.....	.... weken voor / na
Meer dan 4 personen in de omgeving ? Vul dan alleen in hoeveel personen:				

c. Wanneer iemand kinkhoest krijgt wordt vanwege besmettingsgevaar aan **personen in de omgeving** (bijvoorbeeld broertje of zusje) soms antibiotica (penicilline-achtige medicijnen) gegeven om te **voorkómen** dat zij ook kinkhoest krijgen.

Heeft uw kind om bovenstaande reden antibiotica gekregen **vóórdat** hij/zij kinkhoest kreeg en zo ja, wanneer?

1 ❒ ja, op |__|__| -- |__|__| -- |1|9|__|__|
dag maand jaar
2 ❒ nee

Kinkhoestklachten en ziektebeloop

Dit onderdeel gaat over klachten en ziekteverschijnselen en heeft **alléén betrekking op die periode waarin uw kind kinkhoest heeft (gehad)**. Wanneer u de datum of een schatting van een datum weet, wilt u deze dan invullen?

14. **Wanneer** begonnen de kinkhoestklachten bij uw kind?

|_|_| -- |_|_| --|1|9|_|_|
dag maand jaar
2 ❒ weet ik niet

15. Heeft uw kind gehoest?

1 ❒ ja, gedurende de dag en nacht
2 ❒ ja, alleen gedurende de dag
3 ❒ ja, alleen gedurende de nacht
4 ❒ nee ⇨ *ga verder naar vraag 21*
5 ❒ weet ik niet

16. Heeft uw kind ook in **aanvallen** gehoest met tussen de hoestaanvallen geen of af en toe hoesten?

1 ❒ ja
2 ❒ nee ⇨ *ga verder naar vraag 20*
3 ❒ weet ik niet ⇨ *ga verder naar vraag 20*

17. Heeft uw kind ook hoestaanvallen (gehad) met gierende inademing (*ook wel **'kinken'** genoemd)*?

1 ❒ ja
2 ❒ nee
3 ❒ weet ik niet

18. **Hoelang** heeft uw kind hoestaanvallen gehad?

1 |_|_| weken
2 ❒ op dit moment nog hoestaanvallen maar tot nu toe |_|_| weken
3 ❒ weet ik niet

19a. Wat was het **meeste aantal** hoestaanvallen **overdag**?

1 ❒ |_|_| keer
2 ❒ weet ik niet

b. Wat was het **meeste aantal** hoestaanvallen **'s nachts**?

1 ❒ |_|_| keer
2 ❒ weet ik niet

c. **Hoelang** duurde zo'n hoestaanval maximaal?

1 |_|_| minuten
2 ❒ weet ik niet

20. Kwam het voor dat uw kind **ná hoesten** of een **hoestaanval:**
(meerdere antwoorden mogelijk)

1 ❒ moest overgeven/braken
1 ❒ last had van ademnood
1 ❒ blauw aanliep
1 ❒ (bijna) flauwviel
1 ❒ geen van bovenstaande

21. Had uw kind zogenaamde **'stille aanvallen'** (zonder hoestaanval) waarbij het kind wit/bleek wegtrok en niet/slecht reageerde?
(Dit kan vooral voorkomen bij erg jonge patiëntjes)

1 ❒ ja
2 ❒ nee
3 ❒ weet ik niet

22a. Heeft uw kind in de periode dat hij/zij kinkhoest had ook koorts gehad?

1 ❒ ja
2 ❒ nee
3 ❒ weet ik niet

b. Zo ja, wat was de hoogst gemeten tempertuur?

1 |__|__|,|__| °C
2 ❒ weet ik niet

c. Zo ja, heeft uw kind ook koortsstuipen gehad?

1 ❒ ja
2 ❒ nee
3 ❒ weet ik niet

23a. Heeft uw kind gewicht verloren in de periode dat hij/zij kinkhoest had?

1 ❒ ja
2 ❒ nee
3 ❒ weet ik niet

b. Zo ja, hoeveel?

1 |__|__| kg
2 ❒ weet ik niet

24. Zijn er complicaties van kinkhoest opgetreden bij uw kind? *(meer antwoorden mogelijk)*

1 ❒ longontsteking.
1 ❒ andere luchtwegaandoeningen, namelijk:.....
1 ❒ middenoorontsteking
1 ❒ epileptische aanvallen
1 ❒ andere aandoeningen zenuwstelsel, namelijk:.....
1 ❒ bloeding in het oogwit.
1 ❒ bloedend tongriempje
1 ❒ breuk (bijvoorbeeld liesbreuk, navelbreuk) namelijk.....
1 ❒ anders, namelijk.....
.....
1 ❒ geen van bovenstaande

25. Heeft uw kind thuis gehouden omdat hij/zij teveel last had van de kinkhoestklachten?
(dus niet vanwege besmettingsgevaar voor anderen)

1 ❒ ja, 1 dag - 3 dagen
2 ❒ ja, 4 dagen - 7 dagen
3 ❒ ja, 8 dagen - 14 dagen
4 ❒ langer dan 14 dagen
5 ❒ op dit moment nog thuis
maar tot nu toe |__|__| dagen
6 ❒ nee

26a. Hoe vaak heeft u een huisarts geraadpleegd in verband met de kinkhoestklachten van uw kind?

1 ❒ niet geraadpleegd
2 ❒ 1-2 keer
3 ❒ 3-4 keer
4 ❒ 5 keer of vaker
5 ❒ ik weet niet hoe vaak

b. Heeft u een kinderarts of andere specialist geraadpleegd in verband met de kinkhoestklachten van uw kind?

1 ❒ ja
2 ❒ nee

c. Zo ja, welk(e) specialisme(n)?
(meer antwoorden mogelijk)

1 ❒ kinderarts
1 ❒ keel- ,neus- en oorarts
1 ❒ anders, namelijk.....

27a. Is uw kind opgenomen geweest in het ziekenhuis in de periode dat hij/zij kinkhoest had/heeft?

1 ❒ ja, vanwege kinkhoest
2 ❒ ja, vanwege kinkhoest en voor iets anders, namelijk

.....

3 ❒ nee, voor iets anders namelijk

.....

4 ❒ nee, niet opgenomen

b. Zo ja, hoeveel dagen is uw kind opgenomen?

1 ❒ ja, |__|__| dagen
2 ❒ is op dit moment nog opgenomen maar tot nu toe |__|__| dagen

28a. Heeft uw kind op dit moment nog kinkhoestklachten?

1 ❒ nee
2 ❒ ja
3 ❒ weet ik niet

b. Zo nee, wanneer waren de klachten helemaal voorbij?

|__|__| -- |__|__| --|1|9|__|__|
dag maand jaar

c. Zo ja, wat zijn op **dit moment** de klachten?

.....

.....

.....

29. Wanneer uw huisarts of specialist uw kind medicijnen tegen kinkhoest voorschreef; welke medicijnen waren dit dan? (*meerdere antwoorden mogelijk, indien bekend graag de naam vermelden*)

1 ❒ antibiotica.....
1 ❒ pijnstillers.....
1 ❒ medicijn tegen hoesten.....
1 ❒ anders.....
1 ❒ ja, wel medicijnen voorgeschreven, maar ik weet niet welke
1 ❒ nee, geen medicijnen voorgeschreven
1 ❒ weet ik niet

Inentingsgegevens

In dit laatste deel van de vragenlijst worden vragen gesteld over (kinkhoest) inentingen die uw kind mogelijk heeft gehad.

30. Is uw kind ingeënt tegen kinkhoest?

1 ❒ ja
2 ❒ nee
3 ❒ weet ik niet

31. Heeft u een vaccinatieboekje of vaccinatiekaart van uw kind?

1 ❒ ja
2 ❒ nee, ⇨ *ga verder naar vraag 33*

Zo ja, wilt u deze dan gebruiken bij het beantwoorden van de volgende vraag?

32. Volgens het gangbare inentingsprogramma is het gebruikelijk dat inenting tegen kinkhoest samen (in één prik) met inenting tegen difterie, tetanus en polio gebeurd. Dit gebeurt op een leeftijd van drie, vier, vijf en elf maanden. Soms wordt hier echter van af geweken. In het inentingsboekje staat meestal geschreven **welk** vaccin **wanneer is** gegeven.

Wilt u bij deze vraag de **soort inenting** aankruisen (DKTP, DTP en K) die vermeld staat in het vaccinatieboekje of de vaccinatiekaart van uw kind? (Andere inentingen zoals Hib, bof, rode hond of mazelen hoeven niet te worden vermeld)

DKTP: difterie, **kinkhoest**, tetanus en polio
DTP: difterie, tetanus, polio
K: kinkhoest

Soort inenting			**Datum van inenting**	
1e.	❒ DKTP of ❒ DTP	of ❒ onbekend	__ | __ -- | __ --	1 9 __
			dag maand	jaar
2e.	❒ DKTP of ❒ DTP	of ❒ onbekend	__ | __ -- | __ --	1 9 __
			dag maand	jaar
3e.	❒ DKTP of ❒ DTP	of ❒ onbekend	__ | __ -- | __ --	1 9 __
			dag maand	jaar
4e.	❒ DKTP of ❒ DTP	of ❒ onbekend	__ | __ -- | __ --	1 9 __
			dag maand	jaar
5e.	.....	of ❒ onbekend	__ | __ -- | __ --	1 9 __
			dag maand	jaar
6e.	.....	of ❒ onbekend	__ | __ -- | __ --	1 9 __
			dag maand	jaar

33. Indien uw kind **niet is ingeënt** tegen kinkhoest, wat is hiervan dan de reden? *(meer antwoorden mogelijk)*

1 ❒ nog te jong

1 ❒ vanwege ziekte/medische redenen op advies van arts

1 ❒ angst voor bijwerkingen/ziekte

1 ❒ vanwege principiële weigering (geloofsovertuiging) geen deelname aan het rijksvaccinatieprogramma

1 ❒ andere reden, namelijk .....

.....

1 ❒ weet ik niet

1 ❒ niet van toepassing

34a. Stuurt u ook de bijgesloten **toestemmingsverklaring** met de vragenlijst mee? 1 ❒ ja 2 ❒ nee

b. Zo ja, in welke plaats is uw kind voor het laatst ingeënt in verband met het vaccinatieprogramma? Plaats: .....

35. Heeft u nog opmerkingen over de vragenlijst of over dit onderzoek?

.....

.....

.....

.....

.....

.....

U bent klaar met het invullen van de vragenlijst.

Wilt u de vragenlijst nog een keer doorlopen om te kijken of u alle vragen juist hebt beantwoord?

Wilt u de ingevulde vragenlijst en eventueel de ondertekende toestemmingsverklaring retourneren in de bijgevoegde envelop (een postzegel is niet nodig)?

Hartelijk dank voor uw medewerking!

Appendix XI Questionnaire Notification study (≥16 years)

B	

VRAGENLIJST

VOOR PATIENTEN MET KINKHOEST

Toelichting bij de vragenlijst

Deze vragenlijst bestaat uit 30 vragen. Het invullen van de vragenlijst duurt ongeveer 20 minuten. De vragenlijst begint met enkele algemene vragen. Vervolgens worden vragen gesteld over uw gezondheid en welke klachten u had door de kinkhoest. Tot slot worden enkele vragen gesteld over de inentingen die u heeft gehad. Deze laatste gegevens over de inenting kunt u het beste uit het vaccinatieboekje of vaccinatiekaart halen.

Bij de meeste vragen staan meerdere antwoordmogelijkheden. Wilt u het antwoord aankruisen dat voor u van toepassing is òf het beste bij uw situatie past? Bij een aantal vragen is er ruimte waar u zelf een antwoord in kunt vullen.

Bij sommige vragen wordt gevraagd naar een datum (bijvoorbeeld wanneer uw klachten begonnen). Wij kunnen ons voorstellen dat u de **exacte** datum niet meer weet. Misschien kunt u in dat geval met behulp van een kalender of agenda toch een geschatte datum invullen. Op de nummertjes bij de antwoorden hoeft u niet te letten, deze dienen alleen voor onze verwerking.

Voorbeeld

Stel bijvoorbeeld dat de vragenlijst gaat over een vrouw, geboren 24-03-76. De vrouw vult de vragenlijst in en dan ziet het voorbeeld er als volgt uit:

Wat is uw geslacht?

1 ❒ man
2 ■ vrouw

Wat is uw geboortedatum?

|2|4| -- |0|3| --|1|9|7|6|
dag maand jaar

Dit geldt voor het invullen van alle vragen in de vragenlijst.
Wilt u bij **alle** vragen (tenzij anders vermeld) een antwoord aankruisen?

Veel succes bij het invullen van de vragenlijst!

Algemeen

Hieronder worden enkele algemene vragen gesteld over uw persoonsgegevens en over het huishouden waar u deel van uitmaakt.

1. Wie vult deze vragenlijst in?

1 ❒ patiënt zelf

2 ❒ iemand anders, namelijk:

.....

(invullen bijvoorbeeld ouder, echtgenoot)

2. Wanneer vult u deze vragenlijst in?

|_|_| -- |_|_| --|1|9|_|_|

dag maand jaar

3. Wat is uw geslacht?

1 ❒ man

2 ❒ vrouw

4. Wat is uw geboortedatum?

|_|_| -- |_|_| --|1|9|_|_|

dag maand jaar

5a. Uit hoeveel personen bestaat het huishouden waarvan u deel uit maakt (inclusief uzelf)?

|_|_| personen

b. Met welke personen woont u momenteel samen?

(meer antwoorden mogelijk)

1 ❒ met mijn partner

1 ❒ met mijn ouder(s)/ verzorger(s)

1 ❒ met een kind of kinderen van tot 4 jaar

1 ❒ met een kind of kinderen van 4 tot 10 jaar

1 ❒ met een kind of kinderen van 10 tot 16 jaar

1 ❒ met een persoon of personen van 16 jaar en ouder

1 ❒ met geen van bovenstaande personen

GEZONDHEID EN ZIEKTEGEGEVENS

Dit onderdeel van de vragenlijst bevat vragen over uw gezondheid doorgemaakte ziekten **in de periode vóórdat u kinkhoest kreeg.**

6. Wat was uw gewicht voordat u kinkhoest kreeg?

1 |__|__| kg

2 ❒ weet ik niet

7. Wat is uw lengte?

1 |__|,|__|__| meter

2 ❒ weet ik niet

8. Had u reeds een ziekte of aandoening, **vòòrdat u** kinkhoest kreeg? (*meer antwoorden mogelijk*)

1 ❒ Astma, chronische bronchitis of COPD

1 ❒ Andere longziekte, namelijk.....

1 ❒ Ontsteking van de neusbijholte, voorhoofdsholte of kaakholte

1 ❒ Allergie, met allergische reacties van de luchtwegen bijvoorbeeld door hooikoorts en huisstofmijt

1 ❒ Allergie, met allergische reacties van de huid bijvoorbeeld door contacteczeem

1 ❒ Allergie, met allergische reacties veroorzaakt door bepaalde voedingsmiddelen bijvoorbeeld koemelkeiwit

1 ❒ Ziekte van zenuwstelsel (bijvoorbeeld epilepsie), namelijk.....

1 ❒ Ontwikkelingsstoornis, namelijk.....

1 ❒ Andere ziekten of aandoeningen, namelijk.....

.....

1 ❒ Geen ziekten of aandoeningen

9a. Heeft u **eerder** kinkhoest gehad en wanneer?

1 ❒ ja

2 ❒ nee

b. Zo ja, wanneer?

|1|9|__|__| jaar

10a. Zijn er andere personen in uw omgeving die kinkhoest hebben gekregen in de periode van **6 weken vóór** tot **6 weken ná** uw eerste ziektedag?

1 ❒ ja
2 ❒ nee, ⇨ *ga verder naar vraag 11*

b. Zo ja, welke personen waren dat, wanneer, op **welke leeftijd** en **waar** in de omgeving?

Voorbeeld 1: uw buurjongen van 8 jaar had kinkhoest 4 weken voordat u zelf kinkhoest kreeg.
Voorbeeld 2: uw kind van 6 maanden kreeg kinkhoest 3 weken nadat u zelf kinkhoest kreeg.

Indien meer dan 4 personen in uw omgeving kinkhoest hebben (gehad) vult u dan **alleen** het aantal personen in onderin de tabel.

	Persoon in omgeving	Leeftijd van die persoon	Waar in de omgeving	Tijdsduur **vóór** of **na** het moment dat u kinkhoest kreeg
Voorbeeld 1	*buurjongen*	*8 jaar/~~maanden~~*	*buurt*	*4 weken voor / ~~na~~*
Voorbeeld 2	*kind*	*6 ~~jaar~~/maanden*	*gezin*	*3 weken ~~voor~~/na*
Persoon 1:	.....	..... jaar/maanden	.....	.... weken voor / na
Persoon 2:	.....	..... jaar/maanden	.....	.... weken voor / na
Persoon 3:	.....	..... jaar/maanden	.....	.... weken voor / na
Persoon 4:	.....	.... jaar/maanden	.....	.... weken voor / na
Meer dan 4 personen in de omgeving ? Vul dan alleen in hoeveel personen:				

c. Wanneer iemand kinkhoest krijgt wordt vanwege besmettingsgevaar aan **personen in de omgeving** (bijvoorbeeld broertje of zusje) soms antibiotica (penicilline-achtige medicijnen) gegeven om te **voorkómen** dat zij ook kinkhoest krijgen.

Heeft u om bovenstaande reden antibiotica gekregen **vóórdat** u kinkhoest kreeg?

1 ❒ ja op |__|__| -- |__|__| -- |1|9|__|__|
dag maand jaar
2 ❒ nee

Kinkhoestklachten en ziektebeloop

Dit onderdeel gaat over klachten en ziekteverschijnselen en heeft **alléén betrekking op die periode waarin u kinkhoest heeft (gehad)**. Wanneer u de datum of een schatting van een datum weet, wilt u deze dan invullen?

11. **Wanneer** begonnen bij u de kinkhoestklachten? |_|_| -- |_|_| -- |1|9|_|_|
dag maand jaar
2 ❒ weet ik niet

12. Heeft u gehoest?
1 ❒ ja, gedurende de dag en nacht
2 ❒ ja, alleen gedurende de dag
3 ❒ ja, alleen gedurende de nacht
4 ❒ nee ⇨ *ga verder naar vraag 18*
5 ❒ weet ik niet

13. Heeft u ook in **aanvallen** gehoest met tussen de hoestaanvallen geen of af en toe hoesten?
1 ❒ ja
2 ❒ nee ⇨ *ga verder naar vraag17*
3 ❒ weet ik niet ⇨ *ga verder naar vraag 17*

14. Heeft u ook hoestaanvallen (gehad) met gierende inademing (*ook wel **'kinken'** genoemd)*?
1 ❒ ja
2 ❒ nee
3 ❒ weet ik niet

15. **Hoelang** heeft u hoest**aanvallen** gehad?
1 |_|_| weken
2 ❒ op dit moment nog hoestaanvallen maar tot nu toe |_|_| weken
3 ❒ weet ik niet

16a. Wat was het **meeste aantal** hoestaanvallen **overdag**?
1 |__|__| keer
2 ❒ weet ik niet

b. Wat was het **meeste aantal** hoestaanvallen **'s nachts**?
1 |__|__| keer
2 ❒ weet ik niet

c. Hoelang duurde zo'n hoestaanval maximaal?
1 |__|__| minuten
2 ❒ weet ik niet

17. Kwam het voor dat u **ná hoesten** of een **hoestaanval**:
(meerdere antwoorden mogelijk)
1 ❒ moest overgeven/braken
1 ❒ last had van ademnood
1 ❒ blauw aanliep
1 ❒ (bijna) flauwviel
1 ❒ geen van bovenstaande

18a. Heeft u in de periode dat u kinkhoest had ook koorts gehad?
1 ❒ ja
2 ❒ nee
3 ❒ weet ik niet

b. Zo ja, wat was de hoogst gemeten termperatuur?
|__|__|,|__| °C
2 ❒ weet ik niet

19a. Heeft u gewicht verloren in de periode dat u kinkhoest had?
1 ❒ ja
2 ❒ nee
3 ❒ weet ik niet

b. Zo ja, hoeveel?
1 |__|__| kg
2 ❒ weet ik niet

20. Zijn er complicaties van kinkhoest opgetreden *(meer antwoorden mogelijk)*

1 ❒ longontsteking.

1 ❒ andere luchtwegaandoeningen, namelijk:.....

1 ❒ middenoorontsteking

1 ❒ epileptische aanvallen

1 ❒ andere aandoeningen zenuwstelsel, namelijk:.....

1 ❒ bloeding in het oogwit.

1 ❒ breuk (bijvoorbeeld liesbreuk, navelbreuk) namelijk.....

1 ❒ anders, namelijk.....

1 ❒ geen van bovenstaande

21. Bent u thuis gebleven (van werk/school) omdat u teveel last had van de kinkhoestklachten? *(dus niet vanwege besmettingsgevaar voor anderen)*

1 ❒ ja, 1 dag - 3 dagen
2 ❒ ja, 4 dagen - 7 dagen
3 ❒ ja, 8 dagen - 14 dagen
4 ❒ langer dan 14 dagen
5 ❒ op dit moment nog thuis maar tot nu toe |__|__| dagen
6 ❒ nee

22a. Hoe vaak heeft u uw huisarts geraadpleegd in verband met kinkhoest?

1 ❒ niet geraadpleegd
2 ❒ 1-2 keer
3 ❒ 3-4 keer
4 ❒ 5 keer of vaker
5 ❒ ik weet niet hoe vaak

b. Heeft u een andere specialist geraadpleegd in verband met uw kinkhoestklachten?

1 ❒ ja
2 ❒ nee

c. Zo ja, welk(e) specialisme(n)? *(meer antwoorden mogelijk)*

1 ❒ keel-,neus- en oorarts
1 ❒ anders, namelijk.....

23a. Werd u opgenomen in het ziekenhuis in de periode dat u kinkhoest had/heeft?

1 ❒ ja, vanwege kinkhoest
2 ❒ ja, vanwege kinkhoest en voor iets anders, namelijk
.....
3 ❒ nee, voor iets anders namelijk
.....
4 ❒ nee, niet opgenomen

b. Zo ja, hoeveel dagen bent u opgenomen?

1 ❒ ja, |__|__| dagen
2 ❒ op dit moment nog opgenomen maar tot nu toe |__|__| dagen

24a. Heeft u op **op dit moment** nog kinkhoestklachten?

1 ❒ nee
2 ❒ ja
3 ❒ weet ik niet

b. Zo nee, wanneer waren de kinkhoestklachten helemaal **voorbij?**

|__|__| -- |__|__| -- |1|9|__|__|
dag maand jaar

c. Zo ja, wat zijn op dit moment de klachten?

.....
.....
.....

25. Wanneer uw huisarts of specialist u medicijnen tegen kinkhoest voorschreef; welke medicijnen waren dit dan? (*meerdere antwoorden mogelijk, indien bekend graag de naam vermelden*)

1 ❒ antibiotica.....
1 ❒ pijnstillers.....
1 ❒ medicijn tegen hoesten .....
1 ❒ anders.....
1 ❒ ja, wel medicijnen voorgeschreven, maar ik weet niet welke
1 ❒ nee, geen medicijnen voorgeschreven
1 ❒ weet ik niet

Inentingsgegevens

In dit laatste deel van de vragenlijst worden vragen gesteld over (kinkhoest) inentingen die u mogelijk heeft gehad.

26. Bent u ingeënt tegen **kinkhoest**?

1 ❒ ja
2 ❒ nee
3 ❒ weet ik niet

27. Heeft u een vaccinatieboekje of vaccinatiekaart?

1 ❒ ja
2 ❒ nee ⇨ *ga verder naar vraag 29*

Zo ja, wilt u deze dan gebruiken bij het beantwoorden van de volgende vragen?

28. Volgens het gangbare inentingsprogramma is het gebruikelijk dat inenting tegen kinkhoest samen (in één prik) met inenting tegen difterie, tetanus en polio gebeurd. Dit gebeurt op een leeftijd van drie, vier, vijf en elf maanden. Soms wordt hier echter van af geweken. In het inentingsboekje staat meestal geschreven **welk** vaccin **wanneer is** gegeven.

Wilt u bij deze vraag de **soort inenting** aankruisen (DKTP, DTP en K) die vermeld staat in uw vaccinatieboekje of de vaccinatiekaart? Andere inentingen zoals Hib, bof , rode hond of mazelen hoeven niet te worden vermeld.

DKTP: difterie, **kinkhoest**, tetanus en polio
DTP: difterie, tetanus, polio
K: kinkhoest

Soort inenting				**Datum van inenting**
1e.	❒ DKTP	of ❒ DTP	of ❒ onbekend	|__|__| -- |__|__| --|1|9|__|__| dag maand jaar
2e.	❒ DKTP	of ❒ DTP	of ❒ onbekend	|__|__| -- |__|__| --|1|9|__|__| dag maand jaar
3e.	❒ DKTP	of ❒ DTP	of ❒ onbekend	|__|__| -- |__|__| --|1|9|__|__| dag maand jaar
4e.	❒ DKTP	of ❒ DTP	of ❒ onbekend	|__|__| -- |__|__| --|1|9|__|__| dag maand jaar
5e.	.....		of ❒ onbekend	|__|__| -- |__|__| --|1|9|__|__| dag maand jaar
6e.	.....		of ❒ onbekend	|__|__| -- |__|__| --|1|9|__|__| dag maand jaar

29. Indien u **niet bent ingeënt** tegen kinkhoest, wat was hiervan dan de reden? *(meer antwoorden mogelijk)*

1 ❒ vanwege ziekte/ medische redenen op advies van arts

1 ❒ angst voor bijwerkingen/ziekte

1 ❒ vanwege principiële weigering (geloofsovertuiging)

1 ❒ vroeger niet tegen kinkhoest ingeënt

1 ❒ andere reden, namelijk .....

.....

1 ❒ weet ik niet

1 ❒ niet van toepassing

30. Heeft u nog opmerkingen over de vragenlijst of over dit onderzoek?

.....

.....

.....

.....

U bent klaar met het invullen van de vragenlijst.

Wilt u de vragenlijst nog een keer doorlopen om te kijken of u alle vragen juist hebt beantwoord?

Wilt u de ingevulde vragenlijst retourneren in de bijgevoegde envelop? Een postzegel is niet nodig.

Hartelijk dank voor uw medewerking!

Appendix XI Matching notifications data - serodiagnostic data

The notification cases in the study were individually matched with the notification data of the IGZ in 1997. Before matching the IGZ data were matched individually with the serodiagnostic data of the LIS. Thus, the notification data of the IGZ included for some observations also data about the serodiagnostics. In that case more information was often available for example an extra day of birth. The total number of observations in the notification data in the study was 544 and in the IGZ data 2671.

The matching was performed in the following steps:

1. matching first four characters of the last name, date of birth (according to the serodiagnostic data). Result: 247 matches.
2. matching first four characters of the last name, date of birth (according to the notification) Result: 158 matches.
3. matching date of birth (according to the IGZ notifications). Result: 91 matches.
4. matching date of birth (according to the serodiagnostic data). Result: 5 matches
5. matching first four characters of the last name and first four characters of place of residence (according to the serodiagnostic data). Result: 1 matches.
6. matching first four characters of last name and first four characters of place of residence (according to the IGZ notification). Result: 7 matches.
7. matching first six characters of last name. Result: 1 match.
8. matching plausible birthday and last name. Result 4 matches

Records that were matches twice were excluded. All matches were checked on gender, place of residence, day of birth. In total 513 matches.

Appendix XII Gender and vaccination distribution routine notification data

Table 1 shows the number of the cases in the routine notification system during the 4 months that the study was conducted. Overall, about 1034 cases were notified which is about twice the number of cases who participated. The gender distribution in the notification study was comparable with the distribution in the routine notification system. In de older age group more women (63%) were notified compared with men (37%).

Appendix XII shows the vaccination status of notified cases in the period of October 1997 - January 1998 according to the routine system. In the older age group 25% was unvaccinated.

Table 1. Gender of pertussis case in the routine notification system in the period of October 1997 - January 1998

characteristics	age <16 years n=826	age ≥ 16 years n=208	total n=1034
gender			
male	426 (52%)	77 (37%)	503 (49%)
female	400 (48%)	131 (63%)	531 (51%)

Table 2. Vaccination status of notified pertussis cases in the routine system in the period of October 1997 - January 1998 (n=1034)

vaccination status	age <16 years n=826	age ≥ 16 years n=208	total n=1034
unvaccinated	32 (4%)	51 (25%)	83 (8%)
incompletely vaccinated	16 (2%)	1 (1%)	17 (2%)
vaccinated	766 (93%)	141 (68 %)	907 (88%)
unknown	12 (1%)	15 (7 %)	27 (3%)

Appendix XIII Method of diagnosis notified cases

Table 1 Method of diagnoses notified pertussis cases by age group

Diagnostics	age <16 years n=402	age ≥ 16 years n=105	total n=507
serology	281 (70%)	74 (70%)	355 (70%)
clinical / serology	44 (11%)	15 (14%)	59 (12%)
culture	14 (3%)	3 (3%)	17 (3%)
clinical	15 (4%)	1 (1%)	16 (3%)
clinical / epidemiology	10 (2%)	2 (2%)	12 (2%)
epidemiology	6 (1%)	1 (1%)	7 (1%)
culture / serology	4 (1%)	--	4 (1%)
clinical / culture	1 (0%)	--	1 (0%)
serology / epidemiological	1 (0%)	--	1 (0%)
clinical / epidemiology / serology	--	1 (1%)	1 (0%)
unknown	26 (6%)	8 (8%)	34 (7%)
not linked	21 (5%)	8 (8%)	29 (6%)

Table 2 Result serological diagnostics in notified pertussis cases by age group

Result serology	age <16 years n=236	age ≥ 16 years n=65	total n=301
proved (two-point serology)	65 (28%)	12 (18%)	77 (26%)
suspect (one-point serology)	155 (66%)	46 (71%)	201 (65%)
no indication for pertussis	1 (0.4%)	1 (2%)	2 (1%)
unknown	15 (6%)	6 (9%)	2 (1%)