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TEN YEAR REPORT

Pertussis in Göteborg study area

Technical report October 1, 1997 until December 31, 2007, including enhanced surveillance January 1, 2003 until December 31, 2007, with an executive summary

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1 Executive Summary

1.1 Introduction

In Sweden pertussis vaccination was withdrawn in 1979. During 1980 to 1995 laboratory confirmed pertussis was voluntarily reported from all bacteriological laboratories with full personal identifiers. Following a 17 year hiatus without general vaccination, pertussis vaccination of infants was again included in the national vaccination program after licensure of the new acellular vaccines in January 1996, and pertussis was included in the Communicable Disease Act in 1997.

Since then, the national epidemiology of pertussis in all age-groups is studied annually by analysing the obligatory reporting. Cases of pertussis, either clinically suspected or/and laboratory confirmed by culture, PCR or serology are reported to the Swedish Institute for Infectious Disease Control through a computer-linked reporting system (SmiNet). Basic data in this routine reporting system include, for example, information on origin of report (clinician or laboratory) and the national registration numbers (NRN), but there are limited or no clinical and/or vaccination data available from the routine reports. Laboratory reports include laboratory method and (normally) date of sampling and/or date of positive result. The NRN are individually unique Swedish person identifiers that include information on date of birth, sex and current registered place of residence including county.

The epidemiology of pertussis in vaccinated cohorts, i.e. children born from 1996, has been studied since October 1st 1997 within an enhanced surveillance project, identifying laboratory verified cases through the routine reporting system. NRN and date of laboratory sample has been entered into a separate study base, with addition of detailed data on vaccination status and clinical outcome as collected by structured interview. For a general summary of the enhanced surveillance project, see the main ten-year report [1].

One area of Sweden, called the Göteborg study area (Table 5, section 2.2), located within the region of Västra Götaland (VG), was excluded from the enhanced follow-up until 2003 because pertussis surveillance was already done in this study area within a clinical trial setting [2, 3], including a mass vaccination project. In all 56 percent of children in the area, born 1990 through 1995, were vaccinated within this project during the years 1997-2000 [4].

During four to five of the most recent ten years it has been obvious from the yearly national epidemiological reports that there have been more laboratory reported cases of pertussis in the VG region in relation to population size than in the rest of Sweden, Figure 1. The number of cases in this region was clearly in excess of the expected numbers during 2001-2004, with a marked peak in 2004.

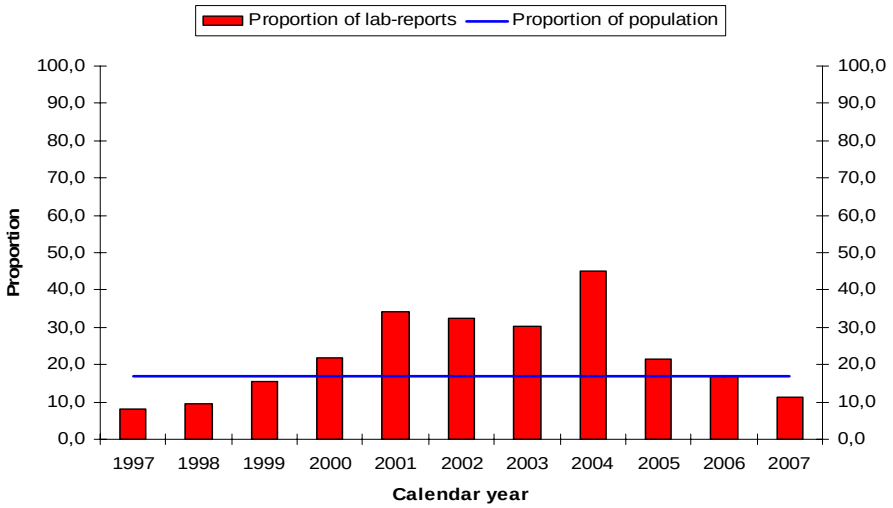

Figure 1 Proportion of number of laboratory reported cases of pertussis from the region of Västra Götaland (based on numbers in table 37B), and proportion of population in this region during the years 1997-2006 (based on mean population figures from Statistics Sweden).

The VG region consists of two parts, i.e. the Göteborg study area and the rest of the VG region, representing about 47% and 53% of the region population, respectively. During the process of collecting

and analysing the enhanced surveillance data, it became obvious that most of the pertussis reports in the VG region were from the part representing the Göteborg study area, Table 1. For other areas of Sweden there were only minor differences when comparing proportions of laboratory reported cases in relation to proportion of population size ("index"-column of Table 1).

Table 1 Number of laboratory confirmed cases from October 1, 1997 until December 31, 2007 for children born January 1, 1996 until December 31, 2007, in different areas of Sweden in relation to population size of the area. Population figures (2007 mid year population) are taken from Table 4 in the main ten-year report [1] and numbers of laboratory confirmed cases are taken from Section 3 of the present report. The "measure" in column "Index" is percent of laboratory confirmed cases divided by percent of population in respective area of Sweden.

Area	**Population**		**Laboratory confirmed cases**		**Index**
	Number in 1000	**Percent of total**	**Number**	**Percent of total**	**Percent of cases divided by percent of population**
Göteborg study area	803	8,8	1 237	36.5	4,2
V. Götaland exc. Gbg	811	8,9	242	7,1	0,8
Stockholm	1 933	21,1	543	16.0	0,8
Skåne	1 191	13,0	283	8.4	0,6
"South"	1 174	12,8	329	9,7	0,8
"Middle-east"	1 005	11,0	211	6.2	0,6
"Middle-west"	1 073	11,7	284	8,4	0,7
"North"	1 155	12,6	256	7.6	0,6
Total	9 148	100	3 385	100	1

The excess in reported cases of pertussis from the VG region during the years 2000-2005 (Figure 1) is hence explained by an excess in reports from the Göteborg study area. The aim of the nine year Göteborg report [5] was, therefore, to present detailed pertussis epidemiology data for the Göteborg study area in comparison with the rest of Sweden, and to provide and discuss a list of plausible explanations to the differences noted, with the present report updating this information until December 31, 2007.

In Section 2 of this report we present the enhanced surveillance data for children born January 1, 1996 until December 31, 2007 from the Göteborg study area for the 5-year period January 1, 2003 through December 31, 2007, with comparisons to the rest of Sweden. This section of the Göteborg report include age and vaccination data in relation date of onset of symptoms, and also in relation to detailed clinical information including different case definitions (i.e. different grades of severity of disease).

It is important to realise that we do not have, and can never get, any comparable clinical data for pertussis episodes in Göteborg children during the previous 5 ¼ years. During this period the area was excluded from the enhanced surveillance project and detailed clinical information, including date of onset of symptoms, cannot be collected retrospectively. It is therefore not possible to compare the prospectively collected detailed clinical information from the rest of Sweden during the period October 1, 1997 to December 31, 2002, with corresponding information from the Göteborg study area.

Information on individual vaccination status can, however, be collected retrospectively from medical records, and this was done autumn 2006. Having filled this part of the information gap for the first 5 ¼ years of the enhanced surveillance project, we can present additional analyses and comparisons between the two areas for the whole "ten-year" period, October 1, 1997 until December 31, 2007. These additional analyses are presented in Section 3 of this report and include vaccination data and age at date of the positive laboratory sample. It is to be noted that we cannot perform analyses by varying the case definitions in these analyses – the only "end-point" is a laboratory confirmed case of pertussis.

Comparisons of performance indicators for the vaccination program and efforts to check differences in awareness are included in Section 4, presenting the overall reported data from the region of VG in comparison with the rest of Sweden. Laboratory denominator data are not included in the present Swedish national reporting system, but by courtesy of the county medical officers in VG and some other

regions, we have been able to perform some comparisons of data from laboratories within VG as well as from the Göteborg study area and from the other large cities Stockholm and Malmö-Lund.

The plausible explanations to the high number of laboratory reported cases from the Göteborg study area are discussed in section 1.4.

1.2 Materials and methods

Within the enhanced surveillance project, all culture- or PCR-verified cases of pertussis in Sweden in children born January 1, 1996 until December 31, 2007 were identified from the national computer-linked reporting system. Basic data, i.e. NRN, place of residence and laboratory date were entered into a separate surveillance database. For all children from the Göteborg study area there was also a "flag" entered in the database. Routine reports based on serology or immunofluorescence, and clinical reports without laboratory confirmation were not at all included in the study database. Hence the study database includes information on birth date and sampling date for all culture- or PCR-verified pertussis in children born from 1996, regardless of area of residence – making it possible to calculate age of child at sampling date for all records in the surveillance database.

During the first 5 ¼ years of the enhanced surveillance project, October 1, 1997 until December 31, 2002, children from the Göteborg study area, entered in the surveillance database, were excluded from the follow-up of clinical and vaccination data. Children from the rest of Sweden were followed-up in detail by telephone interviews to parents and child/school health care nurses, if the child was born after 1995 or participated in the nationwide pertussis trial I and II, and had a laboratory-reported episode of pertussis no earlier than October 1, 1997. Vaccination data, as well as detailed clinical data, including information on hospitalisations, complications and antibiotic treatment, were collected and entered in the surveillance database. During the next 5 years of enhanced surveillance, January 1, 2003 until December 31, 2007, also laboratory-reported cases of pertussis from the Göteborg study area were followed-up in detail, if the child was born after 1995. Hence the study database include detailed information from 5-year of enhanced surveillance of children in the Göteborg study area, January 1, 2003 through December 31, 2007, and detailed information from 10-years of surveillance in the rest of Sweden, October 1, 1997 through December 31, 2007.

Thus, for children from the Göteborg study area there was originally no clinical data or vaccination history collected as supplementary information to the positive laboratory reports with a sampling date from October 1, 1997 until December 31, 2002. To fill this "gap" we have, in 2006-2007, retrospectively collected the vaccination information for almost all of these children. This was mainly done by collecting the individual vaccination data from the individual medical records by telephone to the Child or School Health Care nurses, and also by collecting the individual vaccination data from the computerised files of the Göteborg mass vaccination study.

In summary, data for Göteborg study area children, born January 1, 1996 until December 31, 2007, are presented in three ways in this report:

i) 5-years of enhanced surveillance information (i.e. with detailed clinical and vaccination data for episodes with onset of disease from January 1, 2003 until December 31, 2007), including a comparison with the corresponding data from the rest of Sweden (**Section 2**)
ii) 10-years of information on age at sampling date for all culture or PCR-reported cases of pertussis for the whole ten-year period (laboratory sampling date between October 1, 1997 until December 31, 2007, without clinical and vaccination data), including a comparison with the corresponding data from the rest of Sweden (**Section 3, Part 1**)
iii) 10 years of information on vaccination status at sampling date for all culture or PCR-reported cases of pertussis for the whole ten-year period, with retrospectively collected ivaccination data for the Göteborg children with culture- or PCR reports dated October 1, 1997 until December 31, 2002 and prospectively collected vaccination data for episodes dated January 1, 2003 until December 31, 2007, (i.e. individual vaccination data for the whole 10-year period, without any clinical data) including a comparison with the corresponding data from the rest of Sweden, (**Section 3, Part 2**).

1.2.1 Göteborg study area, vaccines and vaccination

The Göteborg study area is defined as the city of Göteborg and nine additional surrounding municipalities (Table 5, section 2.2), corresponding to the study area of the Göteborg pertussis vaccine trial and mass vaccination project [2, 3, 4]. Eight of these municipalities and the city of Göteborg are geographically located within the region of Västra Götaland, whereas the 9th municipality (Kungsbacka) is located within the county of Halland.

In the Göteborg study area, a trivalent one-component DTPa* with only PT* (DiTeKik®, SSI) was used within the ordinary vaccination program from January 1996 and until spring 1999, when it was replaced by a pentavalent two-component DTPa-IPV-Hib* with PT and FHA* (Pentavac®, Sanofi Pasteur MSD). During the same period (from 1996 and until spring 2000), there was in this area a mass vaccination project, offering general and free catch-up during the years 1996-1999 by use of monovalent one-component Pa vaccine (Kikhostevaccin, SSI) to all children born in the 1990:s [4].

From 2007 the Swedish vaccination program includes a pre-school and a school-leaving booster against diptheria-tetanus-pertussis to children born from 2002, with a catch-up dose against the three diseases to children born 1995-2001 at 10 years of age [6]. Hitherto no child in the study database has yet reported any booster dose according to the revised schedule prior to the pertussis episode.

1.3 Results

1.3.1 Göteborg enhanced surveillance (Section 2)

During the 5-year period of surveillance, January 1, 2003 until December 31, 2007, there were 582 followed episodes of laboratory confirmed pertussis within the Göteborg area among 581 children born January 1, 1996 until December 31, 2007, with onset of symptoms from January 1, 2003 until December 31, 2007. Detailed vaccination history and information on coughing period, including duration of spasmodic cough, is available for all 582 episodes of pertussis. Data on hospital stay and complications are available for 580 episodes. Information on antibiotic treatment is available for 580 episodes, whereof 54 were excluded from analyses because of incomplete antibiotic course or deviation from vaccination schedule. The remaining 526 were used in the statistical analyses of treatment during the episode.

1.3.2 Göteborg additional analyses (Section 3)

These analyses include the whole 10-year period October 1, 1997 until December 31, 2007. There were 625 culture- or PCR-reported cases of pertussis during the 5 ¼ year period when the Göteborg study area was not included in the enhanced surveillance, i.e. from October 1, 1997 and until December 31, 2002. Individual vaccination status was retrospectively collected for all but 7 of these children. The analyses, in Part 1, also include the 582 cases mentioned in section 1.3.1, and 30 cases from the enhanced period where vaccination data and clinical details was lacking.

In all the ten-year Part 1 analyses include 1 237 laboratory reported cases in the Göteborg area from October 1, 1997 until December 31, 2007 in children born January 1, 1996 until December 31, 2007. Detailed vaccination data are available for 1 200 (97.0%) of these cases, included in the Part 2 analyses.

1.3.3 Age-specific incidence in relation to vaccination data and clinical outcome

Tables 12-15 of Section 2 present total number of person-years, number of laboratory confirmed pertussis cases and incidence figures with 95% confidence intervals for children in Göteborg study area and the rest of Sweden as well as relative risk results comparing the two areas. All results are presented in age-groups corresponding to the vaccination intervals in the vaccination program and also for one-year age-groups from 1 year of age. These analyses are based on episodes during the 5-year period January 1, 2003 until December 31, 2007.

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* DTPa = diphtheria-tetanus-acellular pertussis vaccine,
DTPa-IPV-Hib = diphtheria-tetanus-acellular pertussis-inactivated polio and Haemophilus influenzae type b vaccine,
PT = pertussis toxoid, FHA = filamentous haemagglutinin

In all tables an intent-to-treat or a per-protocol approach was used, with analyses according to age and vaccination status at date for onset of cough during the pertussis episode. The number of children with pertussis during the period between second and third dose, and the number of toddlers with pertussis after three doses represent "vaccine failures". There is at present no consensus on the upper age limit for the definition of vaccine failure after primary immunisation. We have therefore included all children born January 1, 1996 through December 31, 2006 with culture- or PCR-reported pertussis after three doses, regardless of age at episode.

The analyses are also done according to different pertussis case definitions. The two main definitions used are all laboratory reported cases regardless of severity (Table 12 and 14), and the WHO definition of typical pertussis (Table 13 and 15), i.e. 21 days of more of paroxysmal cough (See Section 2.1.3). In addition, some analyses are performed using the current reporting definitions of 2 weeks or more of coughing any kind.

We refer to section 2.6 for the detailed results of the comparisons between the two areas. As a summary: We observe larger risks of being a reported pertussis case for children in the Göteborg study area compared to the rest of Sweden in nearly all comparisons (Table 12 – Table 15). Table 2 present some other comparisons between the two areas, with data from Section 2 and done here as a complement to the results in Section 2. About 9.5% of newborns in Sweden during the years 1996-2007 were born in the Göteborg study area and in the last column, named "Index", the percentage of pertussis cases in the Göteborg study area of total number of cases in Sweden, is divided by 9.5.

Table 2 Some comparisons, related to different background or outcome parameters, of number of pertussis cases occurring during January 1, 2003 until December 31, 2007, for children born from January 1, 1996 until December 31, 2007, in Göteborg in relation to the rest of Sweden.

Category of pertussis case & First Table in Section 2 where comparison data are presented		Total number of cases in Sweden	The Göteborg study area		
			Number of cases	Percent of total number of cases in Sweden	Index Percent of total number adjusted to population size of newborn children
All reported cases[1]	**Table 7**	1 705	582	34.1	3.6
Unvaccinated children	**Table 8**	479	96	20.0	2.1
Unvaccinated children ≥ 1 y	**Table 9**	96	16	16.7	1.8
Vaccinated with one dose	**Table 10**	172	51	29.7	3.1
Vaccinated with two doses[2]	**Table 10**	124	79	63.7	6.7
Vaccinated with three doses[3]	**Table 10**	930	356	42.7	3.8
Cough <14 days - spasmodic or non-spasmodic		66	45	68.2	7.2
No spasmodic cough	**-**	352	199	56.5	6.0
Spasmodic cough ≥21 days[4]	**Table 10**	1 253	326	26.0	2.7

For the 5-year period of follow-up, there were considerable, and statically significant, differences between the two areas comparing laboratory confirmed pertussis cases for whom we have both vaccination and clinical data. For all categories (regardless of parameter chosen for comparison) there are more cases in the Göteborg study area (or fewer cases in the rest of Sweden) taken differences between population sizes into account. In comparison with the total number of reports, some of the proportions (vaccinated with two doses, vaccinated with three doses, cough <14 days, no spasmodic cough) were higher whereas other (unvaccinated children, spasmodic cough 21 days) were lower. Note that the reporting of pertussis in unvaccinated infants and in unvaccinated children aged 1 year or more is approximately twice as high in the Göteborg study area than in the rest of Sweden. Note also that the most marked differences in reporting are in milder cases, i.e. in cases with cough < 14 days or cases with no spasmodic cough at all.

[1] For incidence and relative risk results for different age-groups – see Table 12.
[2] For incidence and relative risk results – see Table 14.
[3] For incidence and relative risk results for different age groups – see Table 14.
[4] For incidence and relative risk results for different age/vaccination-groups – see Table 13 and 15.

A more frequent reporting of milder cases in the Göteborg study area is also reflected by results for hospitalization and complications. The overall rates of hospitalization were higher in the Göteborg study area, but there were proportionally fewer hospital admissions among children with reported pertussis in this area than in the rest of Sweden. The proportions of unimmunised children with laboratory-confirmed pertussis in the Göteborg study area and in the rest of Sweden were respectively 34% and 56%. There was furthermore proportionally fewer episodes with a longer hospital stay in Göteborg study area with 27% (9 of 33) of Göteborg children hospitalized for more than one week whereas 43% (93 of 214) had a hospital stay of one week or more in the rest of the country. Also the proportion of all laboratory reported cases with a complication was lower in the Göteborg study area than in the rest of Sweden, with significant differences in proportions with respiratory complications or dehydration.

Table 3 summarizes the overall incidence per 100 000 person years of culture/PCR-confirmed pertussis, episodes with > 21 days of cough, hospital admissions and complications in the age groups surveyed. The number of events recorded per 100 000 person years in different age groups indicate a significantly higher hospitalization rate in the youngest and unvaccinated infants (below 3 months of age) in the Göteborg study area in comparison with the rest of Sweden, but the incidence of hospitalizations in children vaccinated with one dose or more was similar in the two areas. The complication rates were, however, higher in the Göteborg study area also after one dose or more.

Table 3. Incidence of all reported culture/PCR-confirmed cases of pertussis, reported cases with >21 days of cough, hospital admissions and complications in children born from January 1, 1996 until December 31, 2007 and followed from January, 2003 until December 31, 2007, in the Göteborg study area and in the rest of Sweden (95% confidence interval within parenthesis).

	Incidence per 100 000 person years (95% C.I.)							
	Culture/PCR-confirmed pertussis		Episodes with >21 days of cough		Hospital admissions		Complications	
Age groups	Göte-borg	Rest of Sweden	Göte-borg	Rest of Sweden	Göte-borg	Rest of Sweden	Göte-borg	Rest of Sweden
0 - <3 months	561 (439–708	229 (202-257)	324 (233-440)	204 (179-230)	245 (167-348)	170 (146-195)	142 (85-225)	104 (86-124)
3 - <5 months	489 (351-663)	163 (136-193	215 (128-339)	146 (132-189)	72 (26-156)	69 (52-90)	84 (34-172)	38 (25-54)
5 - <12 months	307 (246-377)	28 (22-35)	114 (78-160)	21 (16-28)	3.4 (0.1-19.2)	6.0 (3.4-9.8)	21 (8-45)	4.1 (2.1-7.4)
≥12 months	100 (91-111)	18 (17-20)	62 (54-70)	15 (13-16)	0.8 (0.2-2.3)	0.3 (0.1-0.5)	7.7 (5.1-11.0)	1.7 (1.3-2.2)

Interestingly, there were no significant differences in the overall frequency of antibiotic treatment in infant cases (90% and 88%) or in children with pertussis at age 1 year or more (52% and 47%). However, the proportions of infants treated in the age-groups 3-<5 months and 5-<12 months, were slightly higher in the Göteborg study area as compared to the rest of Sweden, Table 22. The current recommendation is to prescribe antibiotics to all infants with pertussis, already as post-exposure prophylaxis to infants below 6 months and in the form of early treatment to infants aged 6-12 months. As already noted in the main report, antibiotic treatment within a week after onset of coughing was associated with significantly shorter duration of period with paroxysmal coughing.

1.3.4 Age-specific incidence in relation to national vaccination schedule

Tables 12 (Section 2) and 25 (Section 3) present total number of person-years, total number of laboratory confirmed pertussis cases and incidence figures with 95% confidence intervals for children in the Göteborg study area and the rest of Sweden, divided into age-groups corresponding to the vaccination intervals in the national vaccination program. This table presents data for a 5- year period, January 1, 2003 until December 31, 2007, while table 25 presents data from the overall ten-year period October 1, 1997 until December 31, 2007. In both tables an intent-to-treat approach was used, i.e. all children were included regardless of whether they were vaccinated or not, and also regardless of severity of disease.

In spite of different methods for calculation of age, the same kind of decline pattern was seen in the 5-year surveillance group (Table 12) and in the additional ten-year analyses (Table 25). In both tables, the

highest incidence in the Göteborg study area and in the rest of Sweden were reported in the youngest age-groups, with a marked decline from 5 months of age in the rest of Sweden and a slight decline in this age-group in the Göteborg study area, and in both areas a further decline from 12 months of age.

In the Göteborg study area the decline continued until a lowest incidence at 3 years, but Göteborg children at this age still had a 5.2 times higher risk of being reported as a laboratory verified case of pertussis as compared to the rest of the country. From this age there was in Göteborg a slight increase until a maximum after infancy at about 6-8 years of age. This is in contrast to the rest of Sweden, where age-specific incidence rates dropped more markedly during the infancy year and remained at this low level until a slight increase from about 5-6 years. In each age group, but that for nine year of age, children living in the Göteborg study area were at a much higher risk for being reported as a laboratory confirmed case of pertussis compared to children living in the rest of the country. The same pattern is found in the other incidence tables of section 2 and 3, e.g. Table 14 and Table 32.

1.3.5 Age-specific incidence per calendar year

Table 24 (Section 3.3) summarizes the age at laboratory report, and the reporting year, for all 1 237 Göteborg cases as well as for 2 148 pertussis reports from the rest of Sweden during the ten-year period of follow-up. Table 4 provides age-specific incidence, by calendar year of laboratory diagnosis, based on the counts in table 24. Denominator data were derived from Statistics Sweden per calendar year (mid-point population counts for the municipalities included in the Göteborg study area, table 5, section 2.2).

Table 4 Age-specific incidence rates of culture- or PCR-confirmed cases of pertussis from October 1, 1997 until December 31, 2007, by attained age (in years) and calendar year of laboratory diagnosis, among children born January 1, 1996 until December 31, 2007. Age is calculated at date for the positive sample.

			1997	**1998**	**1999**	**2000**	**2001**	**2002**	**2003**	**2004**	**2005**	**2006**	**2007**
Göteborg study area	**Year of age**	**0**	141	154	498	789	596	1 007	459	1 186	252	156	94
		1	*103*	82	177	673	223	356	100	406	114	40	10
		2		*45*	59	248	295	306	127	301	65	10	20
		3			*136*	257	212	225	24	185	78	11	10
		4				*226*	152	200	83	331	46	11	22
		5					*135*	257	35	486	71	12	34
		6						*225*	105	533	166	24	12
		7							*112*	469	142	47	36
		8								*405*	94	47	0
		9									*23*	12	0
		10-11										*112*	*8*
Sweden except Göteborg	**Year of age**	**0**	114	95	159	190	72	140	76	177	133	90	76
		1	*15*	21	18	25	15	13	9	17	12	10	5
		2		*18*	34	19	13	29	10	25	7	13	5
		3			*55*	34	16	19	7	13	16	8	6
		4				*59*	19	32	15	24	18	9	9
		5					*22*	33	12	30	23	19	5
		6						*57*	19	32	34	21	22
		7							*13*	48	44	24	21
		8								*80*	37	21	15
		9									*69*	17	23
		10-11										*6*	*8*

Since the data collection started on October 1, 1997, and ended on December 31, 2007, the person-time accrued in the underlying populations in 1997 was multiplied by 0.25 (representing 3/12 year of observation). In the calendar years when the studied cohort first entered the various strata of attained age,

the calendar observation period for this age group was, on average, 1/2 year. For the "transition" age groups, in *italics in the table,* the denominators are multiplied by 0.5.

Figure 1 and table 4 show that there was a marked increase in age-specific incidence in infants already in 1999 for children in the Göteborg study area, i.e. during the last phase of the mass vaccination project, with some increase also in those above 1 year. From the year of 2005 the age-specific incidences in the Göteborg study area have decreased, the levels are, however, still higher than in the rest of the country.

The age-specific incidence rates in earlier birth cohorts than children born after 1995 are not known in the Göteborg study area, since the reports of communicable diseases are only grouped at county level in the national database SmiNet and since those age-groups are not covered by the enhanced surveillance project. The 1997-2006 age-specific incidence rates for the whole region of Västra Götaland (with an overall population of about twice that of Göteborg) are shown in figures 7-8, Section 4.

1.3.6 Pertussis incidence in Göteborg area before and after 1996

Although data from routine notifications according to the communicable disease act are available only for the Västra Götaland region (not for the Göteborg study area), some information from this area is available: Considering that the Göteborg efficacy trial [2] and the Stockholm I efficacy trial [7] were related in time and study design, including case ascertainment routines, the rates of culture-confirmed cases in the placebo-groups of the two trials can be compared. The Göteborg trial started 3-4 months before Stockholm I, and the follow-up in the Göteborg study area stopped about 6 months before the follow-up was terminated in Stockholm, rendering the Göteborg study a slightly shorter follow-up period. The Göteborg placebo group included 1726 children, with 154 culture confirmed cases reported during the follow-up (8.9%). The corresponding group in Stockholm included 2574 children, and 296 culture-confirmed cases were detected (11.5%). Taking the slightly shorter follow-up in the Göteborg study area into account, we consider the incidence of culture-confirmed cases similar in the two trials.

By courtesy of dr Birger Trollfors, we have information on number of positive samples per month at the Göteborg bacteriological laboratory, catchment area mainly Göteborg, from 1986 to March 2001, figure 2. The figure also includes numbers of positive samples for the rest of Sweden (data from figure A of the main report [1] subtracted with the Göteborg data). The number of Göteborg reports for these years seems proportionate to the population of the Göteborg study area, with a scale on the right x-axis is 1/10 of the scale of the left x-axis, corresponding to the fact that the Göteborg study area has about 1/10 of the Swedish population.

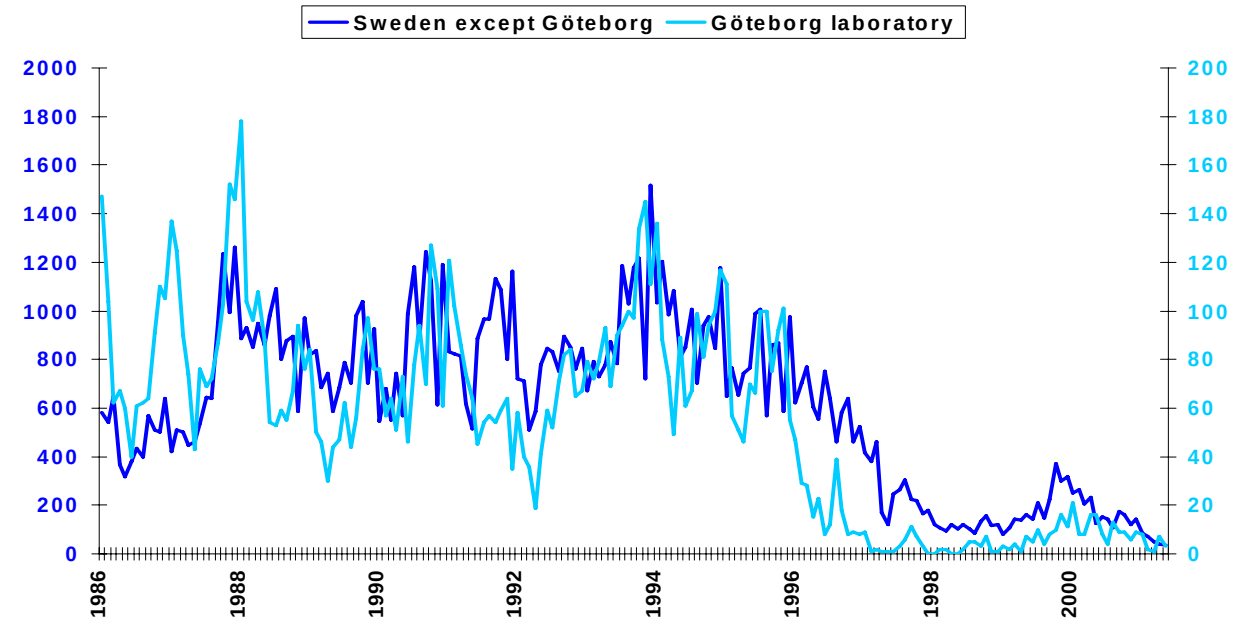

Figure 2 Number of culture- and PCR-confirmed pertussis cases per month area from January 1986 to March 2001 reported from microbiological laboratories in Sweden except the Göteborg laboratory, and from the Göteborg laboratory.

1.4 Discussion

In general, there has been a dramatic decrease in the incidence of pertussis in Sweden after introduction of acellular pertussis vaccines in 1996, Figure 2, and the overall incidence of reported pertussis has since 2000 stabilized at a low level corresponding to the incidence rates in the late sixties when an efficacious whole-cell DTP was used. However, there are still variations in incidence rates over time and geographically. During four to five of the most recent ten years there were more laboratory reported cases of pertussis in the Göteborg study area of the Västra Götaland region in relation to population size than in the rest of Sweden, with a maximum during the year 2004, Figure 1. The aim of the present report is to present detailed pertussis epidemiology data from the Göteborg study area in comparison with the rest of Sweden, and to provide and discuss a list of plausible explanations to the differences noted.

The present technical report from the Göteborg study area summarises

- the 5-year of enhanced surveillance from this area in comparison with the corresponding information from the rest of Sweden, including age-specific calculations by use of date of onset of symptoms (Section 2)
- the 10-year age-specific estimates of pertussis incidence (laboratory confirmed cases) by use of sampling date for both Göteborg and the rest of Sweden, including the 10-year age-specific calculations of pertussis in vaccinated children by use of the retrospectively collected and validated vaccination data (Section 3).

A comparison of number of laboratory confirmed pertussis reports in children born after 1995 during the 10 year period, taking population size into account, indicate only minor differences between different areas of Sweden outside the Göteborg study area. Therefore it is not worth the effort to perform extensive comparisons of the Göteborg study area with for instance the other "large city areas", e.g. Stockholm or Skåne.

As shown in Tables 25-27, Section 3.4, the age-specific incidence rates of confirmed pertussis during the 10 year period is 5-20 times higher in the Göteborg study area compared to the rest of the country, irrespective of period and vaccine use. The vast majority of the Göteborg reports are from the outbreak years 2000-2004, with 30% of the reports (368/1237) reported during the peak year 2004.

The age-specific incidence in unvaccinated infants was significantly higher in the Göteborg study area in comparison with the rest of Sweden, and all incidence tables in sections 2 and 3 demonstrate much higher age-specific incidence rates, compared to the rest of Sweden, in most age-groups above 5 months of age who have received at least two doses of a pertussis vaccine prior to the pertussis episode. This observation holds regardless of whether monocomponent or two-component vaccine was given prior to the positive pertussis episode and regardless of severity of the disease.

Note that the sections 3.3-3.7 only give overall information on the number of culture- and PCR-confirmed cases of pertussis in children born in 1996 or later during the nine year-period, with no details of severity at onset of the pertussis episode. From the 5 year enhanced surveillance period (including the peak year 2004) it seems that significantly more mild cases are reported from the Göteborg study area, as indicated by shorter duration of cough and spasmodic cough, and by lower proportion of hospitalisations and complications among the cases reported in this area in comparison to the corresponding proportion among laboratory reported cases from the rest of Sweden. In fact, the relatively small difference between the proportion of cases meeting the WHO case definition in vaccinated and unimmunised children in the rest of Sweden is not in accordance with data in the randomised controlled trials in 1992-5 and 1993-96, and hence suggests an underreporting of mild cases among vaccinated children in these areas [1].

Section 4 further describes the reporting system in Sweden. A higher proportion of cases are laboratory-verified in the region of Västra Götaland in comparison with the rest of Sweden, but this small difference cannot on its own explain the observed differences. There is also a slight difference in use of laboratory methods, since the Göteborg laboratory was among the first in Sweden to implement PCR technique for detection of *Bordetella pertussis*, although many other laboratories today use the PCR in routine reporting. The time difference in implementation can probably, but only to a small extent, contribute to the higher number of cases reported from the VG region during parts of the nine year period.

Laboratory denominator data, provided by courtesy of the dept of communicable diseases in the region of Västra Götaland, Stockholm and Malmö, indicate that there is a higher sampling rate in relation to population size in the VG region, but there are no differences in the number of samples yielding a positive result. There is, however, a difference within the VG region with more samples submitted to the Microbiological Laboratory in Göteborg, with Göteborg city and surrounding communities as main catchment area, than in the rest of the VG region.

There are no indications that there are any differences in terms of delivery of the national vaccination program. The timing and coverage were similar in the Göteborg study area in comparison to the rest of Sweden.

The overall vaccination program did, however, differ in this region during the first 3-4 years after 1996 since free catch-up was offered to all and given to 56% of all children up to 7 years of age. Free catch-up vaccination was not offered to children born in 1990-1995 in other parts of Sweden. Also, the monocomponent vaccine which was used in the Göteborg study area during 1996-1999, both for vaccination of infants and for the catch-up vaccination 1996-2000 was not used anywhere else in Sweden. Following a transition period, all children in the Göteborg study area were from late spring 2000 vaccinated with a pertussis vaccine which is used also in other parts of Sweden (in about 50% of counties).

It is obvious from the data in Sections 2 and 3 that there are much more reports of laboratory-verified pertussis from the Göteborg study area than from the rest of Sweden. This local increase in incidence was not noted within the Göteborg mass vaccination project because the local epidemiological monitoring stopped when the project stopped in early spring 2000. Unfortunately this coincided with the first phase of the outbreak, at the time was not known. This means that the catch-up vaccinations in fact were withdrawn in a situation when normally additional vaccinations are introduced rather than discontinued.

In summary: The present observational study cannot explain the excess of reports in the Göteborg study area during the years 2000-2004, both among unvaccinated and partly vaccinated infants and among vaccinated children in different age-groups. Noteworthy is that the age-specific incidences in infants, i.e. the age-group most likely to reflect ongoing circulation of pertussis, indicate that the outbreak started already during the last phase of the mass vaccination project in 1999-2000, with rapidly increasing age-specific incidences in infants until peaks with more than 1,000/100,000 infant years during the years 2002 and 2004, whereafter the outbreak declined. These maximum age-specific incidence rates in infants were about five times higher than in the rest of the country, where peaks of 191 and 177/100,000 person years were noted during the years 2000 and 2004. It is therefore likely that there is a true difference in pertussis incidence indicating a large and long-lasting outbreak of the pertussis disease during these years in the Göteborg study area, as indicated by high age-specific incidence in unvaccinated as well as in partly vaccinated infants. This outbreak illustrates the importance of long-term follow-up of vaccination strategies, and also that surveillance of pertussis in unvaccinated infants is a useful tool in monitoring trends in the epidemiology of pertussis.

It is known from the literature that epidemics have a facilitating effect on notification by the presence of large numbers of cases in the community, perhaps mediated in part also by press coverage with a possible time difference during the course of the epidemic. Also, outbreak settings may have a different age-distribution when compared to non-outbreak endemic settings [8].A higher level of awareness in the Göteborg study area was indicated during the period 2003-2007 by the higher proportion of more mild cases than in the rest of Sweden and also by the lower proportion of hospitalization rate among unvaccinated infants with pertussis in the Göteborg area. We do, however, find it unlikely that a higher level of awareness in itself can fully explain the large number of pertussis.

It cannot be excluded that vaccine and vaccination factors, including duration of protection, have contributed to the observed differences in overall number of laboratory cases, in age-specific incidences and in severity of disease as compared to the non-outbreak endemic setting in the rest of the country. As previously noted, the type and design of this observational study cannot address questions on the mechanisms causing these differences between an outbreak setting and ordinary endemic setting.

Mathematic modeling could possibly be one of the additional tools that might help in understanding the

epidemiology of pertussis, but as for the Göteborg study area such an attempt would require information also on pertussis in the catch-up vaccinated cohorts.

Another aspect that cannot be elaborated without further studies is the role of strain variations. From previous years in the enhanced surveillance, when also strain characterisation was included in the study design, it became obvious that strains appear and disappear in waves, with or without differences in clinical pattern of disease. Internationally, pertussis is reemerging in vaccinated populations, and it has been proposed and also provided evidence for that one explanation is antigenic divergence between vaccine strains and circulating strains [9]. In the Netherlands, the resurgence of pertussis has been associated with the rise of B. pertussis strains with a novel promoter region for pertussis toxin (ptxP3) [10]. The P3 strains are found in higher frequency in areas where a monocomponent vaccine is used [Fritz Mooi, personal communication]. As for the Göteborg outbreak it is not known whether or not there were differences in circulating strains as compared to the rest of Sweden. Frozen strains collected from the Göteborg study area during the outbreak years are to some extent available for further characterization studies which could allow comparisons with previous results from the rest of Sweden.

Interestingly, the year 2004 was a peak year also in the rest of the country, and to some extent in other Nordic countries. It is therefore possible that Figure 1 demonstrates the combined effect of a national (or Nordic) peak in 2004 and a large local outbreak in the Göteborg study area during the years 2001-2004.

Noteworthy is that although the situation in the Göteborg study area seems to have returned to normal during 2005-2007, the age-specific incidence in Göteborg infants is still about twice as high as that of what is reported from the rest of the country. We find it likely that a difference of this magnitude could be explained by increased awareness, in contast to the much larger differences noted during the outbreak years.

1.5 Caveats

Our analysis is subject to important limitations. The study design in the enhanced surveillance, including the additional analyses, is open and non-randomised. Case ascertainment is based on routine surveillance of culture- and PCR-confirmed pertussis, with sampling rates varying geographically and over time, according to the awareness of pertussis, local clinical practice, level of suspicion and laboratory experience.

Any comparisons between Göteborg and other areas in Sweden should take this into account and also that the Göteborg study area through careful clinical and laboratory follow-up in clinical trials and mass-vaccination studies performed during more than a decade [2, 3, 4] is likely to have a higher detection rate of pertussis then most parts in the rest of the country. The detection of proportionally milder cases, as demonstrated in Section 2.4, 2.6-2.9, may support this hypothesis. In addition, an outbreak will in itself increase awareness of disease, and hence influence the reporting of milder cases, those where the physician do not normally suspect pertussis.

There are also other problems with surveillance by analysis of laboratory confirmed cases, mainly the differential sensitivity of culture-confirmation in vaccinated compared to unvaccinated individuals, and also differential sensitivity in culture- and PCR-confirmation. Confirmation by PCR has earlier than elsewhere in Sweden replaced culture-confirmation in the Göteborg study area, which may, to some extent, spuriously decrease observed differences between pre and post vaccination periods and may also confound comparisons over time regarding, e.g., waning protection.

Another important limitation is that all vaccinated Göteborg cohorts are not included in the pertussis surveillance. The vaccination regimen in this area included a catch-up strategy involving children born from 1990-1995 and these cohorts are not followed-up with regard to episodes of laboratory-verified pertussis during the ten year period October 1, 1997 to December 31,2007. This means that we cannot address the possible influence of pertussis in these catch-up vaccinated cohorts on the overall situation in the Göteborg study area.

Finally, it needs to be pointed out that this report is clinical, with no analyses of microbiological epidemiology. The influence of *Bordetella pertussis* strain variations is not known, but could be explored by characterization of strains collected both from the Göteborg study area and the rest of Sweden.

2 Enhanced pertussis surveillance in Göteborg study area

2.1 Material and methods

2.1.1 Background, routine reporting system

During 1980 to1995 laboratory confirmed pertussis was voluntarily reported from all bacteriological laboratories with full personal identifiers. Pertussis was included in the Communicable Disease Act in 1997. Since then, all cases of pertussis, either clinically suspected or/and laboratory confirmed by culture, PCR or serology were reported to the Swedish Institute for Infectious Disease Control through a computer-linked reporting system. Basic data in this routine reporting system include for example the unique Swedish person identifier and place of residence including county, but there are limited or no clinical or vaccination data. Laboratory reports include laboratory method and (normally) date of sampling and/or date of positive result.

2.1.2 Enhanced surveillance program

Briefly, all cases of culture or PCR-confirmed pertussis occurring in Sweden in children born since 1996 were identified via the national register of reports according to the Communicable Disease Act from October 1, 1997. All reports except those from Göteborg area between this date and December 31, 2002, were followed-up in detail, i.e. vaccination data as well as clinical data (including data on hospitalisation, complications and antibiotic treatment) were collected, for most of those episodes, by telephone interview according to the same routines as in the nation-wide efficacy trial II [11]. Detailed description of the enhanced surveillance program and the routine reporting system are found in publications [12, 13, 14] and previous progress reports and, with a ten year report updating these results until December 31, 2007 [1].

Pertussis episodes with onset of cough from January 1, 2003 until December 31, 2007 for children in the Göteborg study area were, however, included in the enhanced followed-up. The present report is the second enhanced surveillance progress from this area. The results are presented for episodes occurring in Göteborg study area (582 episodes) respectively in Sweden except Göteborg study area (1 123 episodes) during the 5-year follow-up period from January 1, 2003 until December 31, 2007, for children born from January 1, 1996 until December 31, 2007 for whom we have access to both clinical follow-up and vaccination data, Sections 2.3-2.10.

2.1.3 Pertussis case definitions

An episode of pertussis was defined by (primary case definition) detection of *B. pertussis* by culture- or PCR in a sample obtained >6 months after a previous positive sample, and regardless of symptoms. Typical pertussis was defined as culture- or PCR-confirmed pertussis with twenty-one days or more of spasmodic cough, corresponding to the WHO pertussis case definition of 1991, established for use in the efficacy trials in order to reduce observer bias [15]. Additional analyses according to the EU and WHO case definitions of 2002-2003 [16, 17] have been added as appropriate.

The start of an episode was defined as first day of cough (if no cough, 11 episodes, day of sampling). In the present technical report also analyses according to sampling date have been added.

2.1.4 Person time and incidence calculations

Age-specific incidence rates of pertussis for children born from January 1, 1996 until December 31, 2007 were based on the number of notified pertussis cases during the study period January 1, 2003 until December 31, 2007 as described in the main ten-year report [1].

We computed person time of observation by using data on yearly birth cohort size and months of surveillance for pertussis disease. Person time figures, for Sweden except the Göteborg study area, are taken from the "Ten year report" [1]. Person time figures for the Göteborg study area are based on population figures for municipalities in Sweden during 1996 until 2007 taken from Statistics Sweden http://www.scb.se. To simplify person-time calculations for different cohorts, we used denominator data

based on the following; that the total number of births during a calendar year were equally distributed during the calendar months; that all children were born mid-month and; that for dose-specific incidence rates, vaccinations were given according to the recommended schedule at three, five and twelve month of age.

In addition, annual overall incidences and age-specific incidences of pertussis in the region of Västra Götaland were based on the number of notified culture- or PCR-confirmed pertussis in the whole population of the region and in all age groups, based on age at sampling/notification, and on the corresponding mid-year populations derived from the mean of population figures at two consecutive new years divided by two (data from Statistics Sweden, http://www.scb.se).

2.2 Göteborg study area, vaccines and vaccinated cohorts

2.2.1 Göteborg study area

The Göteborg study area is defined as the city of Göteborg and nine additional surrounding municipalities (Table 5), corresponding to the study area of the Göteborg pertussis trial [2] the same area as the mass vaccination project [4].

Table 5 Municipalities participating in the Göteborg mass-vaccination project

County	Municipality	Mean population 2007
Halland	Kungsbacka	71 493
Västra Götaland	Göteborg	491 630
”	Mölndal	59 184
”	Härryda	32 682
”	Partille	33 657
”	Öckerö	12 242
”	Stenungsund	23 290
”	Tjörn	14 949
”	Ale	26 946
”	Lerum	37 402
Total	**Göteborg study area**	**803 474**

Total population, 2007 (mean population, Statistics Sweden), in the Göteborg study area was about 803 thousand people, i.e. 8.7% of the Swedish population. All but one (Kungsbacka) of the municipalities in the Göteborg study area belong to the region of Västra Götaland, a region with a total population of 1 543 thousand people, i.e. 16.9% of the Swedish population. Thus Västra Götaland can be divided in two parts, municipalities participating or not participating in the Göteborg mass-vaccination project, with population sizes 732 respectively 811 thousand people, i.e. 8.0% and 8.9% of the Swedish population mid 2007.

2.2.2 Vaccines used from 1996 in Göteborg study area

2.2.2.1 General vaccination at 3-5-12 months

Figure 1 of the main ten-year report illustrates the procurement of vaccines by county 1996 –2007 [1]. In the nine municipalities of Västra Götaland and the one (Kungsbacka) of Halland, a trivalent one-component DTPa with only PT (DiTeKik®, SSI) was used within the ordinary vaccination program from 1996 until February 1999, when three municipalities (Ale, Lerum, Kungsbacka) switched to a pentavalent two-component DTPa-IPV-Hib with PT and FHA (Pentavac®, Sanofi Pasteur MSD). The remaining seven municipalities continued with DiTeKik® until February 2000. By March or April 2000 all municipalities in the Göteborg study area used Pentavac®. Children who had received one or two doses with DiTeKik® got the remaining doses with Pentavac® during a period that followed after the change of vaccine.

From 2000 Kungsbacka has followed the routines of Halland. They switched to Infanrix® from the middle of 2000 and used this vaccine during one year, then the corresponding pentavalent two-component combination vaccine Pentavac® (Sanofi Pasteur MSD) was again used for about two years and, “finally” from the middle of 2003 they have used Infanrix® until December 2007.

The corresponding hexavalent vaccines has to a small extent been used to infants at risk for hepatitis B, but most of these were vaccinated with monovalent hepatitis B vaccine administered separately or concomitantly with the pentavalent vaccine.

2.2.2.2 Catch-up vaccination

General and free catch-up by use of monovalent one-component Pa vaccine (Kikhostevacin, SSI) was in the Göteborg study area offered to all children born in the 1990:s during the mass vaccination project. There were also vaccine trials including vaccination with either DiTeKik or Kikhostevaccin, SSI. In all, about 56% of all children until about seven years of age were vaccinated during the years 1996-1999 [4].

2.2.2.3 School boosters

A school booster to children born from 1995-2001 was implemented in autumn 2005. To children born from 2002 this 4th dose of pertussis vaccine is from 2007 given already at 5-6 years of age, and these children will also receive a 5th dose at 14-16 years of age.

2.2.3 Vaccinated birth cohorts in the Göteborg study area

2.2.3.1 Summary of vaccinated birth cohorts

Table 6 summarises vaccines used in different cohorts, and data available in the study database concerning laboratory reports, vaccination data and clinical information. To each cohort there is a short description and an estimate of the vaccination rate.

Table 6 Birth cohorts in the Göteborg study area

1990-5	Children born 1990-1995. Almost 70,000 were vaccinated with DiTeKik® or monovalent one-component vaccine (Kikhostevaccin®, SSI) either within vaccine trials or during the years 1997-2000 within the Göteborg mass vaccination study. Vaccination coverage, with 3 doses in these cohorts, is about 60% (detailed vaccination coverage and information on laboratory reports was collected within the mass vaccination project until spring 2000). Information on laboratory reports in these cohorts is missing thereafter.
1996-8	Children born 1996-1998, vaccinated with DiTeKik®. Vaccine coverage for three doses Pa at 2 years of age is above 98%, according to the statistics from the Child Health Centres from 1999-2001. Information on laboratory reports is lacking for the period 1996-97.09. Detailed clinical information in relation to laboratory reports is missing for the period 199710-20021231.
1999	Children born 1999, vaccinated with DiTeKik® and/or Pentavac®. Vaccine coverage for three doses Pa at 2 years of age is above 98%, according to the statistics from the Child Health Centres from 2002. Detailed clinical information is missing for laboratory confirmed pertussis during the period 1999-20021231
2000-2002	Children born 2000-2002, vaccinated with Pentavac®. Vaccine coverage for three doses Pa at 2 years of age is above 98%, according to the statistics form the Child Health Centres from 2003-2005. Detailed clinical information is missing for laboratory confirmed pertussis during the period 2000-20021231
2003-2006	Children born 2003-2006, vaccinated with Pentavac®. Vaccine coverage for three doses Pa at 2 years of age is above 98% for the cohorts born 2003-2005, according to the statistics form the Child Health Centres. These are the first one-year birth-cohorts completely covered by the Part 1 analyses in this report.
2007	Children born during 2007, still not fully immunised.

2.2.3.2 Followed birth cohorts within the enhanced surveillance

The analyses include enhanced follow-up from January 1, 2003, until December 31, 2007, of children born from January 1, 1996 until December 31, 2007 and residing in the Göteborg study area at time of pertussis. These children are followed continuously from January 1, 2003 in the same way as children from other parts of the country are followed continuously from October 1, 1997.

2.2.3.3 Birth cohorts in the additional analyses

In Section 3, results from the Göteborg study area are summarized for the whole ten year period and each

annual birth cohort is presented with the corresponding age cohorts from the study areas in the rest of Sweden. Available data from the Göteborg study area are also grouped in two groups, which can be characterized as follows. The 1996-1998 cohort, most infants vaccinated with DiTeKik® during a period when toddlers were catch-up vaccinated with monovalent Pa vaccine, and the 2000-2007 cohort, most infants vaccinated with Pentavac®, without catch-up of older siblings.

2.3 Laboratory confirmed pertussis cases used for the 5 year report

In the beginning of March 2008 there were 615 pertussis episodes entered in the surveillance database with a date for the positive sample from January 1, 2003 until December 31, 2007 for children in the Göteborg study area born January 1, 1996 until December 31, 2007. Four of those children with an onset of cough during 2002 were excluded and for 29 (4.7%) of remaining 611 children clinical data had not been possible to collect. Thus, for 582 episodes in 581 children both clinical and vaccination data were entered in the surveillance database for children in the Göteborg study area with an onset of the episode from January 1, 2003 until December 31, 2007.

There was one child from the Göteborg study area with two pertussis episodes after January 1, 2003, the first one occurred at 9 months and the second episode at 24 months of age.

From other parts of Sweden there were 1 203 pertussis episodes entered in the database with a date for the positive sample from January 1, 2003 until December 31, 2007 for children born January 1, 1996 until December 31, 2007. Eleven of those episodes/children with an onset of cough during 2002 were excluded and for 69 (5.8%) of remaining 1 192 children clinical data had not been possible to collect. Thus, for 1 123 episodes in 1 123 children both clinical and vaccination data were entered in the surveillance database for the episodes for children in other parts of Sweden with an onset of the pertussis episode from January 1, 2003 until December 31, 2007.

In Sections 2.3-2.10, we use data from 582 + 1 123 = 1 705 pertussis episodes to estimate and compare pertussis incidence, severeness of the illness and use of antibiotics for children living in the Göteborg study area respectively in the rest of Sweden. In sections 2.4 – 2.6 we present number of pertussis cases per area, per birth cohort and calendar period and per vaccination status of the child, and the pertussis incidences for different age groups for 1 705 episodes of laboratory confirmed pertussis and we compare the results from the two areas of Sweden. In section 2.7 we present results on hospitalisation for children for whom we have data on length of hospitalisation (1 702). The corresponding results for any complication (1 701) due to the pertussis illness during the pertussis episode and the duration of spasmodic cough (1 705) are found in sections 2.8 and 2.9. Treatment with antibiotics is covered in section 2.10.

There are laboratory reports in the database for nine children who died due to the pertussis illness. Two of these were from Göteborg study area. For ethical reasons the parents of these nine children have not been contacted and hence there are no clinical data collected from the parents. However, vaccination status and gestational age was checked with medical personnel, see main (ten year) report, section 2.17 [1].

2.4 Laboratory confirmed pertussis per calendar period & birth cohort

All 1 705 laboratory confirmed cases of pertussis were divided by the followed birth-cohorts and mentioned calendar periods for onset of cough (or, if no cough - 11 children, whereof 9 from the Göteborg study area - during the episode, for date of the positive sample) as well as on the two areas.

Table 7 Total number of reported laboratory confirmed cases of pertussis from January 1, 2003 until December 31, 2007 for children born January 1, 1996 until December 31, 2007, per birth-cohort, period of onset of cough and area for the pertussis episode.

Birth-cohort	Area	2003	2004	2005	2006	2007	Total
1996	**Sweden except Gbg**	**14**	**60**	**41**	**14**	**3**	**132**
	Göteborg study area	***7***	***34***	***3***	***6***	***0***	***50***
1997	**Sweden except Gbg**	**7**	**25**	**26**	**16**	**13**	**87**
	Göteborg study area	***7***	***36***	***15***	***2***	***1***	***60***
1998	**Sweden except Gbg**	**12**	**34**	**40**	**21**	**13**	**120**
	Göteborg study area	***4***	***41***	***11***	***3***	***0***	***59***

1999	**Sweden except Gbg** ***Göteborg study area***	**8** ***9***	**18** ***39***	**25** ***10***	**12** ***6***	**18** ***1***	**81** ***65***
2000	**Sweden except Gbg** ***Göteborg study area***	**7** ***5***	**21** ***12***	**14** ***4***	**24** ***2***	**17** ***0***	**83** ***23***
2001	**Sweden except Gbg** ***Göteborg study area***	**8** ***8***	**16** ***28***	**13** ***4***	**10** ***1***	**8** ***0***	**55** ***41***
2002	**Sweden except Gbg** ***Göteborg study area***	**15** ***17***	**15** ***32***	**10** ***5***	**8** ***1***	**3** ***3***	**51** ***58***
2003	**Sweden except Gbg** ***Göteborg study area***	**52** ***24***	**40** ***55***	**11** ***11***	**6** ***1***	**7** ***1***	**116** ***92***
2004	**Sweden except Gbg** ***Göteborg study area***	**-**	**116** ***73***	**40** ***18***	**12** ***0***	**7** ***2***	**175** ***93***
2005	**Sweden except Gbg** ***Göteborg study area***	**-**	**-**	**74** ***14***	**14** ***6***	**4** ***0***	**92** ***20***
2006	**Sweden except Gbg** ***Göteborg study area***	**-**	**-**	**-**	**63** ***10***	**22** ***5***	**85** ***15***
2007	**Sweden except Gbg** ***Göteborg study area***	**-**	**-**	**-**	**-**	**46** ***6***	**46** ***6***
Total	**Sweden except Gbg** ***Göteborg study area***	**123** ***81***	**345** ***349***	**294** ***95***	**200** ***38***	**161** ***19***	**1 123** ***582***

2.4.1 Laboratory confirmed pertussis among unvaccinated children

Among 1 705 followed children with laboratory confirmed pertussis, 479 (28.1%) had not received a pertussis vaccine prior to the illness – for episodes in the Göteborg study area there were 96 (16.5%) and for children in Sweden except Göteborg there were 383 (34.1%) unvaccinated children, Table 8.

Table 8 Number of reported laboratory confirmed cases of pertussis from January 1, 2003 until December 31, 2007 for children born January 1, 1996 until December 31, 2007, per birth-cohort, period of onset of cough and area for the pertussis episode among children who had not received any pertussis vaccine before onset of cough.

Birth-cohort	Area	2003	2004	2005	2006	2007	Total
1996	**Sweden except Gbg** ***Göteborg study area***	**0** ***1***	**5** ***1***	**2** ***0***	**1** ***0***	**0** ***0***	**8** ***2***
1997	**Sweden except Gbg** ***Göteborg study area***	**3** ***0***	**5** ***0***	**1** ***0***	**2** ***0***	**1** ***0***	**12** ***0***
1998	**Sweden except Gbg** ***Göteborg study area***	**1** ***0***	**1** ***2***	**0** ***1***	**2** ***0***	**1** ***0***	**5** ***3***
1999	**Sweden except Gbg** ***Göteborg study area***	**4** ***0***	**5** ***2***	**1** ***1***	**1** ***0***	**0** ***0***	**11** ***3***
2000	**Sweden except Gbg** ***Göteborg study area***	**1** ***0***	**6** ***2***	**3** ***0***	**7** ***0***	**1** ***0***	**18** ***2***
2001	**Sweden except Gbg** ***Göteborg study area***	**1** ***0***	**4** ***2***	**3** ***0***	**2** ***0***	**1** ***0***	**11** ***2***
2002	**Sweden except Gbg** ***Göteborg study area***	**5** ***3***	**5** ***0***	**1** ***0***	**1** ***1***	**0** ***0***	**12** ***4***
2003	**Sweden except Gbg** ***Göteborg study area***	**41** ***13***	**16** ***6***	**1** ***1***	**0** ***0***	**0** ***0***	**58** ***20***
2004	**Sweden except Gbg** ***Göteborg study area***	**-**	**77** ***33***	**13** ***6***	**1** ***0***	**1** ***0***	**92** ***39***
2005	**Sweden except Gbg** ***Göteborg study area***	**-**	**-**	**60** ***8***	**5** ***0***	**0** ***0***	**65** ***8***
2006	**Sweden except Gbg** ***Göteborg study area***	**-**	**-**	**-**	**44** ***8***	**12** ***2***	**56** ***10***
2007	**Sweden except Gbg** ***Göteborg study area***	**-**	**-**	**-**	**-**	**35** ***3***	**35** ***3***
Total	**Sweden except Gbg** ***Göteborg study area***	**56** ***17***	**124** ***48***	**85** ***17***	**66** ***9***	**52** ***5***	**383** ***96***

All 497 episodes, but four – three from the Göteborg study area – among the unimmunised children were symptomatic according to the clinical follow-up. The minimum duration of cough, if cough, was 7 days - the median duration was 46 days. Spasmodic cough for 21 days or more (episodes according to the WHO-definition) was reported for 84.84% of the episodes – the median duration was 37 days. For 49 (10.2%) of

the episodes there were no spasmodic cough at all.

There were differences between the two areas. The median duration of cough and spasmodic cough among the 96 children from Göteborg study area was 41 and 26 days. The corresponding figures from Sweden except Gbg were 48 and 38 days. Spasmodic cough for 21 days or more was reported for 61.5% of the Göteborg study area children and for 89.6% of children from the rest of Sweden. No spasmodic cough was reported for 29.2% respectively 5.5% of the episodes. All these differences are statistically significant.

Table 9 shows the age distribution of the laboratory confirmed cases at onset of cough for the unimmunised children. Most of the pertussis cases (69.6%) in this subgroup occurred before three months of age, i.e. before the scheduled first dose of a DTPa-containing vaccine. In the Göteborg study area 74% of the pertussis cases among unvaccinated occurred before 3 months of age and the proportion in the rest of Sweden was 68.7%. There is no statistically significant difference between the two areas (p-value=0.92).

Table 9 Age at onset of cough for 479 laboratory confirmed cases of pertussis from January 1, 2003 until December 31, 2007 per area among unvaccinated children.

		Area				Total	
		Göteborg study area		Sweden except Gbg			
		Number	%	Number	%	Number	%
Age in days at onset of cough	0-30	16	16.7	69	18.0	85	17.7
	31-60	29	30.2	101	26.4	130	27.1
	61-90	26	27.1	93	24.3	119	24.8
	91-120	5	5.2	22	5.7	27	5.6
	121-150	2	2.1	8	2.1	10	2.1
	151-180	0	.0	4	1.0	4	0.8
	181-365	2	2.1	6	1.6	8	1.7
	≥366	16	16.7	80	20.9	96	20.0
Total		96	100.0	383	100.0	479	100.0

2.4.2 Laboratory confirmed pertussis among vaccinated children

Among 1 705 reported children 1 226 (71.9%) had received at least one dose of a pertussis vaccine prior to onset of the pertussis episode - 930 children had received 3-4 doses, 124 had received 2 doses and 172 had received only one dose of pertussis vaccine.

For children in the Göteborg study area 356 (61.1%), 79 (13.6%) and 51 (8.8%) had received three, two or one dose of a pertussis vaccine prior to onset of the pertussis episode. Corresponding figures for Sweden except Gbg were; 574 (51.1%), 45 (4.0%) and 121 (10.8%) – (p-value<0.0001). Thus, relatively more children in the Göteborg study area were vaccinated with two or more doses before the episode. Table 10 give the figures for 1 054 children vaccinated with two or more doses before the episode.

Table 10 Number of reported laboratory confirmed cases of pertussis from January 1, 2003 until December 31, 2007 among children born January 1, 1996 until December 31, 2007 per birth-cohort, period of onset of cough and area for the pertussis episode among children vaccinated with two or more doses.

Birth-cohort	Area	2003	2004	2005	2006	2007	Total
1996	**Sweden except Gbg**	**14**	**55**	**38**	**13**	**3**	**123**
	Göteborg study area	***6***	***33***	***3***	***6***	***0***	***48***
1997	**Sweden except Gbg**	**4**	**20**	**25**	**14**	**12**	**75**
	Göteborg study area	***7***	***35***	***14***	***2***	***1***	***59***
1998	**Sweden except Gbg**	**11**	**33**	**40**	**19**	**12**	**115**
	Göteborg study area	***4***	***39***	***9***	***3***	***0***	***55***
1999	**Sweden except Gbg**	**4**	**13**	**24**	**11**	**18**	**70**
	Göteborg study area	***9***	***36***	***9***	***6***	***1***	***61***

2000	**Sweden except Gbg** ***Göteborg study area***	**6** ***5***	**14** ***10***	**11** ***4***	**17** ***2***	**16** ***0***	**64** ***21***
2001	**Sweden except Gbg** ***Göteborg study area***	**7** ***8***	**11** ***26***	**10** ***4***	**8** ***1***	**7** ***0***	**43** ***39***
2002	**Sweden except Gbg** ***Göteborg study area***	**3** ***12***	**10** ***32***	**9** ***5***	**7** ***0***	**3** ***3***	**32** ***52***
2003	**Sweden except Gbg** ***Göteborg study area***	**2** ***4***	**17** ***44***	**10** ***10***	**6** ***1***	**7** ***1***	**42** ***60***
2004	**Sweden except Gbg** ***Göteborg study area***	**-**	**4** ***17***	**16** ***9***	**11** ***0***	**6** ***2***	**37** ***28***
2005	**Sweden except Gbg** ***Göteborg study area***	**-**	**-**	**0** ***3***	**4** ***6***	**5** ***0***	**9** ***9***
2006	**Sweden except Gbg** ***Göteborg study area***	**-**	**-**	**-**	**3** ***0***	**6** ***2***	**9** ***2***
2007	**Sweden except Gbg** ***Göteborg study area***	**-**	**-**	**-**	**-**	**0** **1**	**0** ***1***
Total	**Sweden except Gbg** ***Göteborg study area***	**51** ***55***	**177** ***271***	**183** ***71***	**114** ***27***	**94** **11**	**619** ***435***

All children but five vaccinated with two or more doses were coughing during the pertussis episode. The minimum duration of cough, if cough, was 4 days – the median duration of cough was 46 days. Spasmodic cough for 21 days or more (WHO-definition) was reported for 67.7% of the episodes compared to 84.8% for the unimmunised children – the median duration in immunised children was 31 days. For 26.7% of the episodes there was no spasmodic cough compared to 10.2% for the unimmunised children.

There were differences between the two areas. The median duration of cough and spasmodic cough among 435 children from Göteborg study area was 41 and 24 days. The corresponding figures from Sweden except Gbg were higher; 48 and 34 days. Spasmodic cough for 21 days or more was reported for 55.4% of the Göteborg children and for 76.4% of children from the rest of Sweden. No spasmodic cough was reported for 35.4% respectively 20.5% of the episodes. All these differences are statistically significant.

2.4.3 Some comparisons between cases from the Göteborg study area and the rest of Sweden

Taken population sizes from 1996 until 2007 and follow-up time from 2003 until 2007 in the two areas into account –9.5% of the total amount of follow-up in the Göteborg study area and 90.5% in the rest of Sweden during 2003-2007 – there were many more pertussis cases are reported in the Göteborg study area for most of the birth cohorts from 1996 and for each of the follow-up years from 2003 until 2006, compared to the number of cases reported in the rest of Sweden both for unvaccinated and vaccinated children.

The overall proportion of children with spasmodic cough for 21 or more days was 61.5% (unvaccinated) and 55.4% (vaccinated) for children in the Göteborg study area and 89.6% respectively 76.4% for children in the rest of Sweden. The proportion of children without spasmodic cough during the pertussis illness was 29.2% (unvaccinated) and 35.4% (vaccinated) in the Göteborg study area and 5.5% respectively 20.5% for children in the rest of the country. Thus, proportionally more "mild" pertussis cases are reported in the Göteborg study area both among unvaccinated and vaccinated children.

2.5 Lab. confirmed pertussis in children born Jan. 1, 1996 until Dec. 31, 2007

For this cohort of children there were 1 705 reports of laboratory confirmed pertussis with an onset of the episode from January 1, 2003 until December 31, 2007 for which we have data on both vaccinations and the clinical outcome. There were 582 cases among children in the Göteborg study area, whereof 96 unvaccinated, and 1 123, whereof 383 unvaccinated, among children in the rest of Sweden, Table 11.

Table 11 Number of reported laboratory confirmed cases from January 1, 2003 until December 31, 2007 per birth-cohort from January 1, 1996 to December 31, 2007, number of vaccine doses prior to the

episode and area of episode. The number of cases with 21 or more days of spasmodic cough is given in parenthesis.

Birth-cohort	No. of doses of pertussis vaccine	Sweden except Göteborg		Göteborg study area		Total
		Not vaccinated No. (≥21)	Vaccinated No. (≥21)	Not vaccinated No. (≥21)	Vaccinated No. (≥21)	No. (≥21)
1996	0	8	-	2	-	10 (9)
	1		1		0	1 (1)
	2		0		1	1 (1)
	3		123		47	170 (127)
1997	0	12	-	0	-	12 (11)
	1	-	0	-	1	1 (1)
	2	-	0	-	0	0 (0)
	3	-	75	-	59	134 (104)
1998	0	5	-	3	-	8 (8)
	1	-	0	-	1	1 (1)
	2	-	0	-	1	1 (1)
	3	-	115	-	54	169 (126)
1999	0	11	-	3	-	14 (12)
	1	-	0	-	1	1 (0)
	2	-	0	-	1	1 (1)
	3	-	70	-	60	130 (93)
2000	0	18	-	2	-	20 (19)
	1	-	1	-	0	1 (1)
	2	-	0	-	0	0 (0)
	3	-	64	-	21	85 (59)
2001	0	11	-	2	-	13 (13)
	1	-	1	-	0	1 (1)
	2	-	0	-	0	0 (0)
	3	-	43	-	39	82 (48)
2002	0	12	-	4	-	16 (13)
	1	-	7	-	2	9 (6)
	2	-	1	-	8	9 (3)
	3	-	31	-	44	75 (42)
2003	0	58	-	20	-	78 (58)
	1	-	16	-	12	28 (18)
	2	-	14	-	38	52 (20)
	3	-	28	-	22	50 (34)
2004	0	92		39		131 (101)
	1	-	46	-	26	72 (55)
	2	-	18	-	21	39 (24)
	3	-	19	-	7	26 (16)
2005	0	65	-	8	-	73 (62)
	1	-	18	-	3	21 (18)
	2	-	4	-	6	10 (3)
	3	-	5	-	3	8 (6)
2006	0	56	-	10	-	66 (63)
	1	-	20	-	3	23 (19)
	2	-	8	-	2	10 (5)
	3	-	1	-	0	1 (0)
2007	0	35	-	3	-	38 (37)
	1	-	11		2	13 (12)
	2	-	0	-	1	1 (1)
	3	-	0	-	0	0 (0)
Total	0	383	-	96	-	479 (406)
Total	1	-	121 (107)		51 (26)	172 (133)
Total	2	-	45 (32)		79 (27)	124 (59)
Total	3	-	574 (441)		356 (214)	930 (655)
Total	0 – 3	383 (347)	740 (580)	96 (59)	486 (267)	1 705 (1 253)

2.6 Person-time & incidence in children born Jan. 1, 1996 until Dec. 31, 2007

See sections 2.11 and 2.13 in the main ten year report [1] and in Appendix 1 for population figures from January 1, 1996 until December 31, 2007 in the two compared areas and section 2.1.4 for general principles for calculation of person time of follow-up. In Sections 2.6-2.10 all person-time of follow-up before January 1, 2003 are excluded. During the remaining 5 year period of follow-up children in the Göteborg study area have been followed for approximately 427 thousand person-years and children in the rest of Sweden for 4 041 thousand years.

Tables in this section present total number of person-years, total number of laboratory confirmed pertussis cases and incidence figures with 95% confidence intervals for children in each of the two areas of Sweden divided in four age/vaccination-groups corresponding to the vaccination intervals in the national vaccination program;
- Before dose 1(<3 months of age);
- Between Dose 1 and Dose 2 (3 - <5 months of age);
- Between Dose 2 and Dose 3 (5 - < 12 months of age);
- Between Dose 3 (12 months of age) and Dose 4 (10 years of age).

The interval after 1 year of age is also divided in one-year age intervals of follow-up for which the same information is given.

The relative risk for a reported laboratory positive pertussis episode in the Göteborg study area compared to the rest of Sweden and a 95% confidence interval for the relative risk is also calculated for each age/vaccination interval.

Four incidence tables are presented: Table 12 presents results for total number of laboratory confirmed pertussis cases, irrespective of clinical status, whereas in Table 13 the same analyses are done for children with 21 or more days of spasmodic cough. The approach in Tables 12-13 is an intent to treat, i.e. the overall effect of the vaccination program is studied by use of two different clinical case definitions. In Tables 14 and 15 corresponding analyses are done for children vaccinated with two or more than two doses prior to onset of cough (vaccine failures). The approach in Tables 14-15 is hence a "per protocol" analyses, i.e. the effect in children who are vaccinated according to the national program is studied.

Table 12 presents all children born from January 1, 1996 until December 31, 2007 who had a pertussis episode with onset of episode between January 1, 2003 and December 31, 2007, i.e. the 582 episodes from Göteborg study area and 1 123 episodes from the rest of Sweden during the 5 year period of enhanced surveillance. In each age group (but one), the number of cases reported from Göteborg were high, in relation to population size in the area, with 202 infant cases and 380 cases in children aged 1 year or more reported in this area. From the rest of Sweden there were 464 infant cases and 659 cases in children aged from 1 year.

The relationship between number of children born in the Göteborg study area and born in the rest of Sweden was about 1 to 10.

Table 12 Children born from **January 1, 1996 until December 31, 2007**, and followed from **January 1, 2003 until December 31, 2007** with observed Culture- or PRC-confirmed *B.pertussis*. We present Person-years of follow-up, Number of laboratory confirmed cases, Incidence per 100 000 person-years of follow-up and Relative risk of having a laboratory-verified episode of *B.pertussis* (for children in Sweden except Gbg (except the Göteborg study area) compared to children in the Göteborg study area in the following age-/vaccine-groups at onset of the pertussis episode; 0-<3 months of age (before Dose 1); 3-<5 months of age (between Dose 1 and 2); 5-<12 months of age (between Dose 2 and 3); and after12 months of age (after Dose 3) in ten age intervals. Age is calculated at the date for onset of cough during the episode (for cases without cough the date for the positive sample is used). Age interval in the heading classifies unimmunised children.

Onset of pertussis episode occurred in Vaccine- or Age-group	Person-years of follow-up	Number of laboratory confirmed cases	Incidence per 100 000 person-years and 95% confidence interval	Relative risk Göteborg compared to Sweden except Ggb
Before Dose 1				
During 0-<3 months of age				
Sweden except Gbg	115 610	263	227 (201-256)	-
Göteborg study area	*12 645*	*71*	*561 (439-708)*	***2.5 (1.9 – 3.2)***
Between Dose1 and 2 or				
During 3-<5 months of age	-	-	-	-
Sweden except Gbg	76 735	151	197 (166-234)	-
Göteborg study area	*8 380*	*58*	*692 (525-895)*	***3.5 (2.6 – 4.8)***
Between Dose 2 and 3 or				
During 5-<12 months of age	-	-	-	-
Sweden except Gbg	266 425	55	21 (16-27)	-
Göteborg study area	*29 010*	*81*	*279 (225-347)*	***13.5 (9.6 – 19.1)***
After Dose 3 and/or				
During 1 year of age	-	-	-	-
Sweden except Gbg	447 500	39	9 (6-12)	-
Göteborg study area	*48 460*	*56*	*116 (87-150)*	***13.3 (8.8 – 20.0)***
During 2 years of age	-	-	-	-
Sweden except Gbg	436 355	48	11 (8-15)	-
Göteborg study area	*46 920*	*41*	*87 (63-118)*	***7.9 (5.2 – 12.1)***
During 3 years of age	-	-	-	-
Sweden except Gbg	426 010	45	11 (8-14)	-
Göteborg study area	*45 425*	*25*	*55 (36-81)*	***5.2 (3.2 – 8.5)***
During 4 years of age	-	-	-	-
Sweden except Gbg	415 885	59	14 (11-18)	-
Göteborg study area	*44 110*	*44*	*100 (73-134)*	***7.0 (4.8 – 10.4)***
During 5 years of age	-	-	-	-
Sweden except Gbg	409 100	75	18 (14-23)	-
Göteborg study area	*43 175*	*46*	*107 (78-142)*	***5.8 (4.0 – 8.4)***
During 6 years of age	-	-	-	-
Sweden except Gbg	408 845	101	25 (20-30)	-
Göteborg study area	*42 680*	*66*	*155 (119-197)*	***6.3 (4.6 – 8.5)***
During 7 years of age	-	-	-	-
Sweden except Gbg	369 930	121	33 (27-39)	-
Göteborg study area	*38 285*	*59*	*154 (117-199)*	***4.7 (3.5 – 6.4)***
During 8 years of age	-	-	-	-
Sweden except Gbg	289 120	94	33 (26-40)	-
Göteborg study area	*29 790*	*27*	*91 (60-132)*	***2.8 (1.8 – 4.3)***
During 9 years of age	-	-	-	**-**
Sweden except Gbg	208 930	58	28 (21-36)	**-**
Göteborg study area	*21 380*	*2*	*9 (1-34)*	***0.3 (0.1 – 1.4)***
During 10 or 11 years of age	-	-	-	**-**
Sweden except Gbg	170 870	14	8 (5-14)	**-**
Göteborg study area	*17 325*	*6*	*35 (13-76)*	***4.2 (1.6 – 11.0)***
All after Dose 3 or During 1 year or later	-	-	-	**-**
Sweden except Gbg	3 582 545	654	18 (17-20)	**-**
Göteborg study area	*377 550*	*372*	*99 (89-109)*	***5.4 (4.8 – 6.1)***

In both Göteborg and the rest of Sweden the highest incidences were reported in the two youngest age-groups, with a marked decline from 5 months of age, and a further decline from 12 months of age. In Göteborg there was a further decline until lowest incidence at 3 years, but even at this age Göteborg children had a 5.2 times higher risk of being reported as a laboratory verified case of pertussis in comparison with the rest of the country. Major differences were also found comparing the two areas for children with 21 or more days of spasmodic cough regardless of vaccination status, Table 13.

Table 13 Children born **from January 1, 1996 until December 31, 2007**, and followed from **January 1, 2003 until December 31, 2007** with observed Culture- or PRC-confirmed *B.pertussis* and **with 21 or more days of spasmodic cough**. We present Person-years of follow-up, Number of laboratory confirmed cases, Incidence per 100 000 person-years of follow-up and Relative risk of having a laboratory-verified episode of *B.pertussis* (for children in Sweden except Gbg (except the Göteborg study area) compared to children in the Göteborg study area) in different age-/vaccine-groups at onset of the pertussis episode. Age is calculated at the date for onset of cough during the episode (for cases without cough the date for the positive sample is used). Age interval in the heading classifies unimmunised children.

Onset of pertussis episode occurred in Vaccine- or Age-group	Person-years of follow-up	Number of laboratory confirmed cases	Incidence per 100 000 person-years and 95% confidence interval	Relative risk Göteborg compared to Sweden except Ggb
Before Dose 1				
During 0-<3 months of age				
Sweden except Gbg	115 610	234	202 (177-229)	-
Göteborg study area	*12 645*	*41*	*324 (232-440)*	***1.6 (1.2 – 2.2)***
Between Dose1 and 2 or				
During 3-<5 months of age	-	-	-	-
Sweden except Gbg	76 735	134	175 (145-205)	-
Göteborg study area	*8 380*	*28*	*334 (222-486)*	***1.9 (1.3 – 3.0)***
Between Dose 2 and 3 or				
During 5-<12 months of age	-	-	-	-
Sweden except Gbg	266 425	42	16 (11-21)	-
Göteborg study area	*29 010*	*29*	*100 (67-143)*	***6.3 (4.0 – 10.2)***
After Dose 3 and/or				
During 1 year of age	-	-	-	-
Sweden except Gbg	447 500	29	6 (4-9)	-
Göteborg study area	*48 460*	*26*	*54 (35-79)*	***8.3 (4.9 – 14.1)***
During 2 years of age	-	-	-	-
Sweden except Gbg	436 355	40	9 (7-12)	-
Göteborg study area	*46 920*	*17*	*36 (21-58)*	***4.0 (2.2 – 7.0)***
During 3 years of age	-	-	-	-
Sweden except Gbg	426 010	33	8 (5-11)	-
Göteborg study area	*45 425*	*13*	*29 (15-49)*	***3.7 (1.9 – 7.0)***
During 4 years of age	-	-	-	-
Sweden except Gbg	415 885	43	10 (7-14)	-
Göteborg study area	*44 110*	*26*	*59 (39-86)*	***5.7 (3.5 – 9.3)***
During 5 years of age	-	-	-	-
Sweden except Gbg	409 100	57	14 (11-18)	-
Göteborg study area	*43 175*	*34*	*79 (54-110)*	***5.7 (3.7 – 8.6)***
During 6 years of age	-	-	-	-
Sweden except Gbg	408 845	84	21 (16-25)	-
Göteborg study area	*42 680*	*48*	*112 (82-149)*	***5.5 (3.7 – 7.6)***
During 7 years of age	-	-	-	-
Sweden except Gbg	369 930	94	25 (21-31)	-
Göteborg study area	*38 285*	*37*	*97 (68-133)*	***3.8 (2.6 – 8.1)***
During 8 years of age	-	-	-	-
Sweden except Gbg	289 120	77	27 (21-33)	-
Göteborg study area	*29 790*	*19*	*64 (38-100)*	***2.4 (1.5 – 4.0)***
During 9 years of age	-	-	-	**-**
Sweden except Gbg	208 930	47	22 (17-30)	**-**
Göteborg study area	*21 380*	*2*	*9 (1-34)*	***0.4 (0.1 – 1.7)***
During 10 or 11 years of age	-	-	-	**-**
Sweden except Gbg	170 870	13	8 (4-13)	**-**
Göteborg study area	*17 325*	*6*	*35 (13-76)*	***4.6 (1.7 – 12.0)***
All after Dose 3 or				
During 1 year or later	-	-	-	**-**
Sweden except Gbg	3 582 545	517	14 (13-16)	**-**
Göteborg study area	*377 550*	*228*	*60 (53-69)*	***4.2 (3.6 – 4.8)***

In Tables 14 and 15 vaccine failures, i.e. children vaccinated with 2 or more doses prior to the laboratory positive pertussis episode, are studied. There were 435 such episodes reported for children from the Göteborg study area, whereof 241 with 21 or more days with spasmodic cough, and 619 reported for children from the rest of the country, whereof 473 with 21 or more days of spasmodic cough.

Table 14 Children born **from January 1, 1996 until December 31, 2007**, and followed from **January 1, 2003 until December 31, 2007** with observed Culture- or PRC-confirmed *B.pertussis* and **vaccinated with two or more doses of a pertussis vaccine** prior to the date for onset of the episode. We present Person-years of follow-up, Number of laboratory confirmed cases, Incidence per 100 000 person-years of follow-up and Relative risk of having a laboratory-verified episode of *B.pertussis* (for children in Sweden except Gbg (except the Göteborg study area) compared to children in the Göteborg study area) in the following age-/vaccine-groups at onset of the pertussis episode; between Dose 2 and 3; and after12 months of age (after Dose 3) in ten age intervals. Age is calculated at the date for onset of cough during the episode (for cases without cough the date for the positive sample is used).

Onset of pertussis episode occurred in Vaccine- /Age-group	Person-years of follow-up	Number of laboratory confirmed cases	Incidence per 100 000 person-years and 95% confidence interval	Relative risk Göteborg compared to Sweden except Ggb
Between Dose 2 and 3				
Sweden except Gbg	266 425	45	17 (12-23)	-
Göteborg study area	*29 010*	*79*	*272 (215-340)*	***16.1 (11.2 – 23.3)***
After Dose 3 and During 1 year of age	-	-	-	-
Sweden except Gbg	447 500	30	7 (5-10)	-
Göteborg study area	*48 460*	*54*	*111 (84-145)*	***16.6 (10.6 – 26.0)***
During 2 years of age	-	-	-	-
Sweden except Gbg	436 355	41	9 (7-13)	-
Göteborg study area	*46 920*	*40*	*85 (61-116)*	***9.1 (5.9 – 14.0)***
During 3 years of age	-	-	-	-
Sweden except Gbg	426 010	38	9 (6-12)	-
Göteborg study area	*45 425*	*23*	*51 (32-76)*	***5.7 (3.4 – 9.5)***
During 4 years of age	-	-	-	-
Sweden except Gbg	415 885	44	11 (8-14)	-
Göteborg study area	*44 110*	*40*	*91 (65-124)*	***8.6 (5.6 – 13.2)***
During 5 years of age	-	-	-	-
Sweden except Gbg	409 100	63	15 (12-20)	-
Göteborg study area	*43 175*	*44*	*102 (74-137)*	***6.6 (4.5 – 9.7)***
During 6 years of age	-	-	-	-
Sweden except Gbg	408 845	92	23 (18-28)	-
Göteborg study area	*42 680*	*62*	*145 (111-186)*	***6.5 (4.7 – 8.9)***
During 7 years of age	-	-	-	-
Sweden except Gbg	369 930	111	30 (25-36)	-
Göteborg study area	*38 285*	*59*	*154 (117-199)*	***5.1 (3.8 – 7.0)***
During 8 years of age	-	-	-	-
Sweden except Gbg	289 120	86	30 (24-37)	-
Göteborg study area	*29 790*	*26*	*87 (57-128)*	***2.9 (1.9 – 4.6)***
During 9 years of age	-	-	-	-
Sweden except Gbg	208 930	55	26 (20-34)	-
Göteborg study area	*21 380*	*2*	*9 (1-34)*	***0.4 (0.1 – 1.5)***
During 10 or 11 years of age	-	-	-	-
Sweden except Gbg	170 870	14	8 (5-14)	-
Göteborg study area	*17 325*	*6*	*35 (13-76)*	***4.2 (1.6 – 11.0)***
All after Dose 3	-	-	-	-
Sweden except Gbg	3 582 545	574	16 (15-18)	-
Göteborg study area	*377 550*	*356*	*94 (85-104)*	***5.9 (5.2 – 6.7)***

Table 15 Children born from **January 1, 1996 until December 31, 2007**, and followed from **January 1, 2003 until December 31, 2007** with observed Culture- or PRC-confirmed *B.pertussis* and **with 21 or more days of spasmodic cough** and **vaccinated with 2 or more doses of a pertussis vaccine** prior to the date for onset of the episode. We present Person-years of follow-up, Number of laboratory confirmed cases, Incidence per 100 000 person-years of follow-up and Relative risk of having a laboratory-verified episode of *B.pertussis* (for children in Sweden except Gbg (except the Göteborg study area) compared to children in the Göteborg study area) in the following age-/vaccine-groups at onset of the pertussis episode; between Dose 2 and 3; and after12 months of age (after Dose 3) in ten age intervals. Age is calculated at the date for onset of cough during the episode (for cases without cough the date for the positive sample is used).

Onset of pertussis episode occurred in Vaccine- /Age-group	Person-years of follow-up	Number of laboratory confirmed cases	Incidence per 100 000 person-years and 95% confidence interval	Relative risk Göteborg compared to Sweden except Ggb
Between Dose 2 and 3				-
Sweden except Gbg	266 425	32	12 (8-17)	-
Göteborg study area	*29 010*	*27*	*93 (61-135)*	***7.8 (4.6 – 12.9)***
After Dose 3 and During 1 year of age	-	-	-	-
Sweden except Gbg	447 500	20	5 (3-7)	-
Göteborg study area	*48 460*	*24*	*50 (32-74)*	***11.1 (6.1 – 20.0)***
During 2 years of age	-	-	-	-
Sweden except Gbg	436 355	33	8 (5-11)	-
Göteborg study area	*46 920*	*16*	*34 (19-55)*	***4.5 (2.5 – 8.2)***
During 3 years of age	-	-	-	-
Sweden except Gbg	426 010	27	6 (4-9)	-
Göteborg study area	*45 425*	*11*	*24 (12-43)*	***3.8 (1.9 – 7.7)***
During 4 years of age	-	-	-	-
Sweden except Gbg	415 885	28	7 (5-10)	-
Göteborg study area	*44 110*	*23*	*52 (33-78)*	***7.7 (4.5 – 13.4)***
During 5 years of age	-	-	-	-
Sweden except Gbg	409 100	46	11 (8-15)	-
Göteborg study area	*43 175*	*32*	*74 (51-105)*	***6.6 (4.2 – 10.4)***
During 6 years of age	-	-	-	-
Sweden except Gbg	408 845	75	18 (14-23)	-
Göteborg study area	*42 680*	*45*	*105 (77-141)*	***5.8 (4.0 – 8.3)***
During 7 years of age	-	-	-	-
Sweden except Gbg	369 930	85	23 (18-28)	-
Göteborg study area	*38 285*	*37*	*97 (68-133)*	***4.2 (2.9 – 6.2)***
During 8 years of age	-	-	-	-
Sweden except Gbg	289 120	70	24 (19-31)	-
Göteborg study area	*29 790*	*18*	*60 (36-95)*	***2.5 (1.5 – 4.2)***
During 9 years of age	-	-	-	**-**
Sweden except Gbg	208 930	44	21 (15-28)	**-**
Göteborg study area	*21 380*	*2*	*9 (1-34)*	***0.4 (0.1 – 1.8)***
During 10 or 11 years of age	-	-	-	**-**
Sweden except Gbg	170 870	13	8 (4-13)	**-**
Göteborg study area	*17 325*	*6*	*35 (13-76)*	***4.6 (1.7 – 12.0)***
All after Dose 3	-	-	-	**-**
Sweden except Gbg	3 582 545	441	12 (11-14)	**-**
Göteborg study area	*377 550*	*214*	*57 (49-65)*	***4.6 (3.9– 5.4)***

2.6.1 Comments to the incidence and risk tables

We noted earlier, section 2.4.1-2.4.3, that there were more "mild" pertussis cases reported for children in the Göteborg study area compared to Sweden except Göteborg, both among unvaccinated and vaccinated

children. For comparison of "severe" cases, only cases with 21 or more days of spasmodic cough were included in Tables 13 and 15.

The pattern of "over-risk" noted for children in the Göteborg study area in Tables 12 and 14 was also seen for typical pertussis, Tables 13 and 15. For example; the relative risk for typical pertussis from 12 months of age was 4.2 (95% C.I. 3.6 – 4.8) for all children and 4.6 (95% C.I. 3.9 – 5.4) for children vaccinated with 3 doses in the Göteborg study area compared to children in Sweden except Göteborg. Thus, there were also more "severe" cases of pertussis reported for children in the Göteborg study area.

Comparing relative risk figures in Table 14 with those in Table 12 the relative risk of having a laboratory-confirmed episode of pertussis was higher in all age groups in Table 14, where unvaccinated children were excluded. The same is true comparing Table 15, where only "severe" pertussis cases for children vaccinated with at least two doses of a pertussis vaccine were included, with Tables 13, where also the unvaccinated "severe" cases were included. Thus, one can conclude that – relatively seen – "fewer" unvaccinated pertussis cases are reported from the Göteborg area compared to Sweden except Göteborg.

Caveats in comparing the two areas of Sweden, as well as different reasons for the large differences observed, are discussed in Section 1.4.

2.7 Hospital admission for pertussis

Data on hospitalisation, defined as at least one night at hospital due to the pertussis disease during the episode, was available for 1 702 of 1 705 children born from January 1, 1996 until December 31, 2007 with an episode from January 1, 2003 until December 31, 2007 in the two areas of Sweden.

2.7.1 Hospital admission and age at the pertussis episode

Table 16 Number of hospital admission/Total number of episodes and percent of pertussis episodes with a hospital admission due to pertussis, by age at onset of cough among children born from January 1, 1996 until December 31, 2007, during surveillance from January 1, 2003 until December 31, 2007.

Hospital admission	0 - < 3 months		3 - <5 months		5 -<12 months		≥12months		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%
Sweden excluding Gbg area	196/265	*74*	53/125	*42*	16/74	*22*	10/658	*2*	275/1122	*25*
Göteborg study area	31/71	*44*	6/41	*15*	1/89	*1*	3/379	*1*	41/580	*7*
Total	227/336	*68*	59/166	*36*	17/163	*10*	13/1037	*1*	316/1702	*19*

Three hundred and sixteen (19%) of 1 702 children had a hospital admission during the pertussis episode and 1 386 had none. "Only" 41 (7.1%) children in the Göteborg study area were hospitalised during the pertussis episode compared to 275 (24.5%) children in the rest of the country, this difference was statistically significant. Hospitalisation rates for children in the Göteborg study area were significantly lower compared to the rates in Sweden except Göteborg in all age groups but the last (Table 16).

Age specific incidence rates of hospitalisation due to pertussis per 100 000 years of follow up in the four age groups are shown in Figure 3 (solid lines). For comparison the figure also gives the age specific incidence rates for all pertussis (irrespective of vaccination status before the episode) in the dotted lines. Person time of follow up for incidence calculations for the four age groups was taken from Table 12.

The age specific incidence rate of hospitalisation due to pertussis is highest, 245 per 100 000 years of follow-up, for children 0-<3 months of age and decreases, by increasing age, to less than 1 per 100 000 years for children above one year of age at the pertussis episode for children in the Göteborg study area.

The age specific incidence rate of hospitalisation due to pertussis, for children in the rest of Sweden, is highest, 170 per 100 000 years of follow-up, for children 0-<3 months of age and decreases, by increasing age, to less than 0.5 per 100 000 years for children above one year of age at the pertussis episode. The incidence rates of hospitalisation in the rest of Sweden were lower than for children in the Göteborg study

area in all age groups and significantly lower only for children in the youngest age-group. However, given an episode of pertussis, more children outside the Göteborg study area had a hospital stay during the pertussis episode.

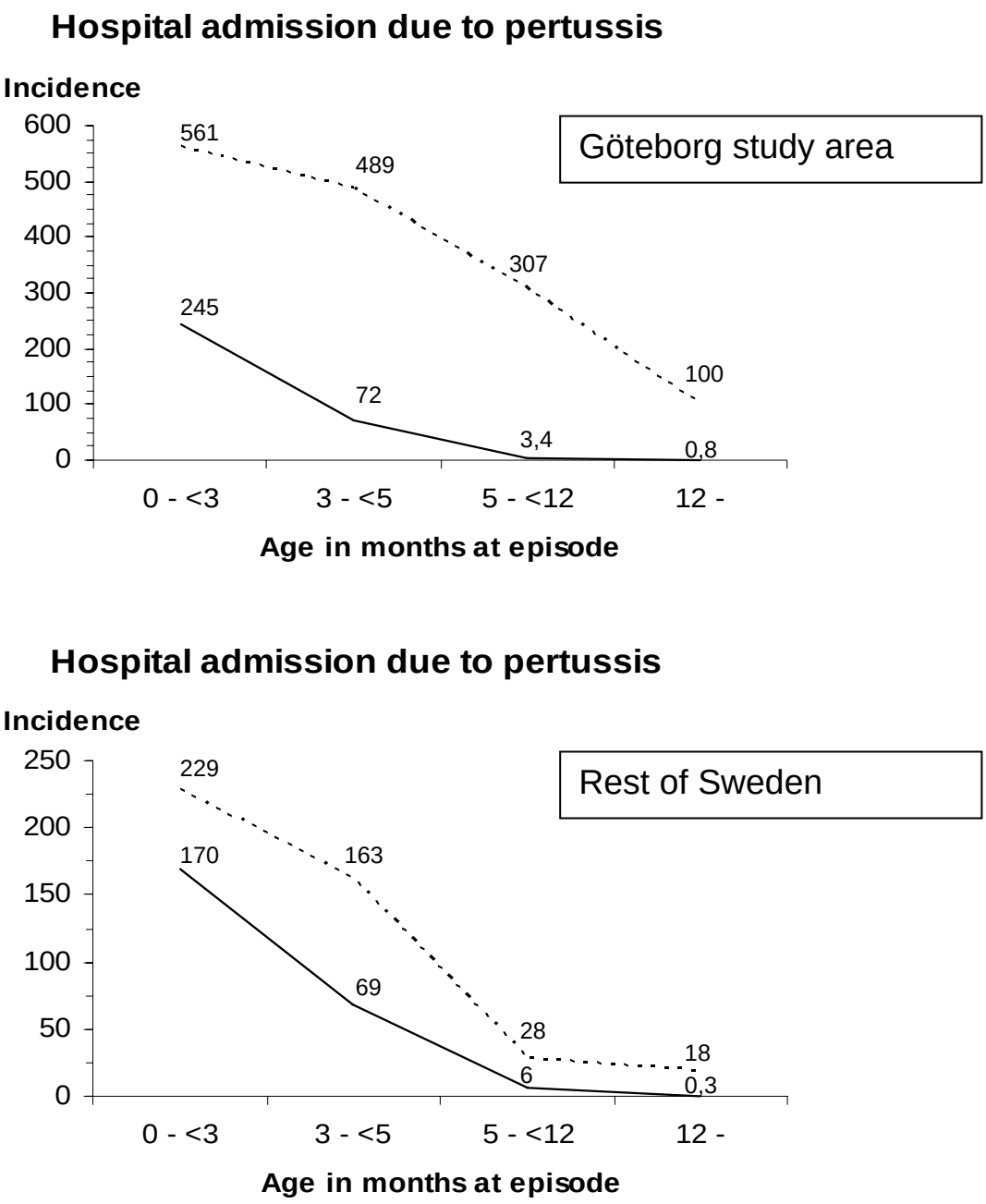

Figure 3 Age specific incidence of hospital admission due to the pertussis disease, solid lines, and age specific incidence of all pertussis, dotted lines, per 100 000 years of follow-up regardless of vaccination status for children born from January 1, 1996 to December 31, 2007 with a laboratory confirmed *B. Pertussis* from January 1, 2003 until December 31, 2007 for children in the Göteborg study area (upper diagram) and children in the rest of Sweden (lower diagram).

Thus, the risk of also suffering a hospital admission due to the disease was highest among children below three months of age at beginning of the pertussis episode. Obviously circulating pertussis in the country has not decreased to a level that offers sufficient protection for the youngest unvaccinated infants.

2.7.2 Duration of hospital stay, age and vaccination status at the pertussis episode

Hospital admissions were also studied in relation to age, duration of hospital stay and vaccination status at start of the pertussis episode. Detailed data are given in Table 17 for children in the Göteborg study area.

Table 17 Duration of hospital stay due to the pertussis among children from the **Göteborg** study area, born from January 1, 1996 until December 31, 2007 and surveyed from January 1, 2003 until December 31, 2007, by age at onset of cough and number of doses of a pertussis vaccine prior to the pertussis episode.

No of doses of a pertussis vaccine prior to the episode			Age of child at beginning of the pertussis episode							Total no. of children
			0-30 days	31-60 days	61-90 days	91-150 days	151-180 days	181-365 days	366- days	
Unimmunised children	**Duration of hospital stay**	**0 days**	9	13	18	5	0	2	16	**63**
		1-7 days	6	10	7	1	0	0	0	**24**
		8- days	1	6	1	1	0	0	0	**9**
	Total no. of children		**16**	**29**	**26**	**7**	**0**	**2**	**16**	**96**
	Total no. and rate of children with a hospital stay		***7 44%***	***16 55%***	***8 31%***	***2 29%***	***0 0%***	***0 0%***	***0 0%***	***33 34%***
Children vaccinated with one dose	**Duration of hospital stay**	**0 days**	-	-	-	30	10	4	3	**47**
		1-7 days	-	-	-	3	0	0	0	**3**
		8- days	-	-	-	1	0	0	0	**1**
	Total no. of children		-	-	-	**34**	**10**	**4**	**3**	**51**
	Total no. and rate of children with a hospital stay		-	-	-	***4 12%***	***0 0%***	***0 0%***	***0 0%***	***4 8%***
Children vaccinated with two or more doses	**Duration of hospital stay**	**0 days**	-	-	-	-	4	68	357	**429**
		1-7 days	-	-	-	-	0	1	2	**3**
		8- days	-	-	-	-	0	0	1	**1**
	Total no. of children		-	-	-	-	**4**	**69**	**360**	**433**
	Total no. and rate of children with a hospital stay		-	-	-	-	***0 0%***	***1 1%***	***3 1%***	***4 1%***
All children regardless of vaccination status	**Duration of hospital stay**	**0 days**	9	13	18	35	14	74	376	**539**
		1-7 days	6	10	7	4	0	1	2	**30**
		8- days	1	6	1	2	0	0	1	**11**
	Total no. of children		**16**	**29**	**26**	**41**	**14**	**75**	**379**	**580**
	Total no. and rate of children with a hospital stay		***7 44%***	***16 55%***	***8 31%***	***6 15%***	***0 0%***	***1 1%***	***3 1%***	***41 7%***

A corresponding table for (1 122) children outside Göteborg study area is not included in the present report because the hospital admission proportions for children outside the Göteborg study area were nearly the same as was reported in Table 11 of the main ten-year report [1] for 2 036 children outside the Göteborg study area. However, the figures that we refer to in the text that follow concern the 1 122 children.

The overall rate of hospital admission for unimmunised children from the Göteborg study area was 34%. For hospitalised children 27% (7 of 33 children) of the hospital admissions had a duration longer than one week, Table 17. The corresponding figures for children from the rest of Sweden were significantly higher. The overall hospitalisation rate was 56% and for hospitalised 42% (93 of 214 children) of the episodes had a duration longer than one week.

The rate of hospital admission among unimmunised children aged 0-30, 31-60 and 61-90 days at beginning of the pertussis episode was 44%, 55% and 31% respectively. For unimmunised children

between 3-<5 and 5-<12 months and above 1 year of age, the rate of hospital admission was lower 29%, 0% and respectively 0% for children from the Göteborg study area, Table 17. Again the rates for children from the rest of Sweden were significantly higher 93%, 71% and 63% for the three youngest age-groups 0-30, 31-60 and 61-90 days and 53%, 30% and 0% in the tree older age-groups.

This downward trend by age in hospitalisation rate was also observed for vaccinated children from the rest of Sweden, both for children vaccinated with only one dose, 121 children whereof 35% (42 children) hospitalised, and for children who have received two or more doses of a pertussis vaccine before the pertussis episode, 618 children whereof 5% (19 children) hospitalised, but the levels for these trends are lower when compared to those for the unvaccinated children – for detailed figures and further discussion of hospitalisation for children outside the Göteborg study area see the main ten-year report [1].

For children from the Göteborg study area there were only 8% (4 of 51 children) vaccinated with only one dose before the episode who were hospitalised and for those with at least two doses of a pertussis vaccine before the episode 1% (4 of 433) were hospitalised – thus the two hospitalisation rates for vaccinated children from the rest of Sweden were also significantly higher. No trend of rate by age was observed for vaccinated children from the Göteborg study area.

2.8 Complications during the pertussis episode

Data on respiratory complication, neurological complication, dehydration with > 5 % loss of weight or other serious complications during the pertussis episode were registered in the database for 1 701 of 1 705 children born from January 1, 1996 until December 31, 2007 with vaccination and follow-up information for a laboratory confirmed pertussis from January 1, 2003 until December 31, 2007.

A respiratory complication (with apnea, n=110, without apnea, n=96) was reported for 206 (12%) and a dehydration for 131 (8%) of the children. Uncommon complications, i.e. neurological complications were reported for 4 (0.2%) children, and other serious complications for 1 child from the Göteborg area. For respiratory complications and dehydration there were statistically significant differences between the Göteborg and the rest of Sweden.

The figures were for respiratory complications 46 (7.9%) and 160 (14.3%), for dehydration 22 (3.8%) and 109 (9.7%), and for neurological complications 1 (0.2%) and 3 (0.3%) for children in the Göteborg area respectively in the rest of Sweden.

2.8.1 Any complication and age at the pertussis episode

To analyse the association between complications during the pertussis episode and age and/or vaccination status of the child at the episode, children were grouped in two groups; children with at least one noted complication and children without any complication during the pertussis episode. Two hundred and eighty children (16.5%) had at least one complication due to the pertussis disease during their pertussis episode and 1 421 (83.5%) had no complication at all.

Table 18 Number of cases with any complication/Total number of episodes and percent with any complication due to pertussis by age at onset of cough among children born from January 1, 1996 until December 31, 2007, during surveillance from January 1, 2003 until December 31, 2007.

Any complication	0 - < 3 months		3 - <5 months		5 -<12 months		≥12 months		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%
Sweden excluding Gbg area	120/265	*45*	29/125	*23*	11/74	*15*	60/657	*9*	220/1121	*20*
Göteborg study area	18/71	*25*	7/41	*17*	6/89	*7*	29/379	*8*	60/580	*10*
Total	138/336	*41*	36/166	*22*	17/163	*10*	89/1036	*9*	280/1701	*16*

Sixty children (10.3%) from the Göteborg study area and 220 (19.6%) from Sweden outside the Göteborg study area had at least one complication during the pertussis episode – this difference was statistically significant. Rates of any complication, due to the pertussis disease for children in the Göteborg study area,

were lower in all age-groups and significantly lower for children from the Göteborg study area in the youngest age-group.

Age specific incidence rates of any complication due to pertussis per 100 000 years of follow up in the four age groups are shown in Figure 4 (solid lines). For comparison the figure also gives the age specific incidence rates for all pertussis (dotted lines).

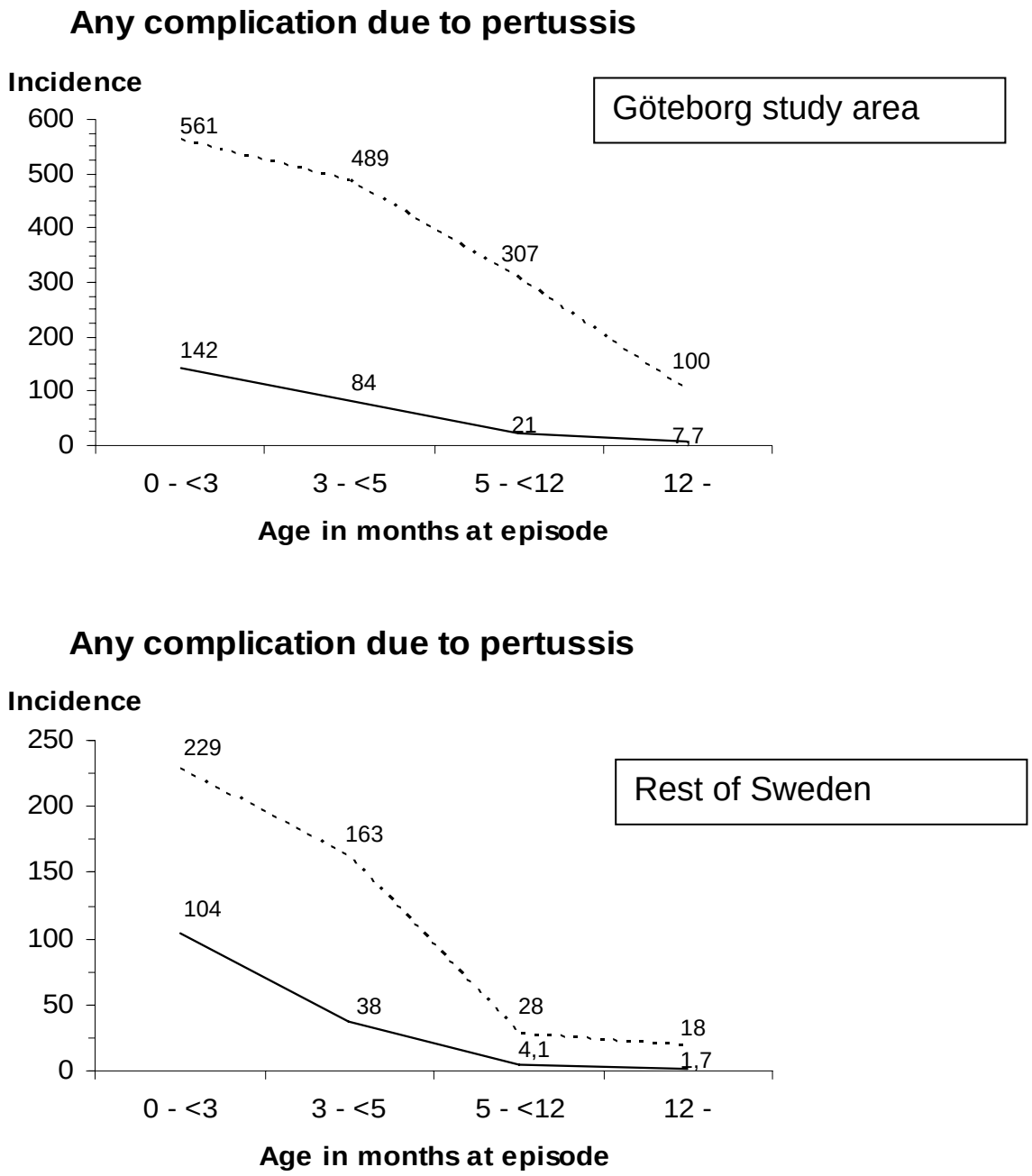

Figure 4 Age specific incidence of any complication due to the pertussis disease, solid lines, and age specific incidence of all pertussis, dotted lines, per 100 000 years of follow-up regardless of vaccination status for children born from January 1, 1996 until December 31, 2007 with a laboratory confirmed *B. pertussis* from January 1, 2003 until December 31, 2007 for children from the Göteborg study area (upper diagram) and children in the rest of Sweden (lower diagram).

The age specific incidence rate of any complication due to pertussis is highest, 142 per 100 000 years of follow-up, for children 0-<3 months of age and decreases, by increasing age, to 7.7 per 100 000 years for children above one year of age at the pertussis episode, for children in the Göteborg area.

The age specific incidence rate of any complication due to pertussis, among children in the rest of Sweden, is highest, 104 per 100 000 years of follow-up, for children 0-<3 months of age and decreases, by increasing age, to less than 2 per 100 000 years for children above one year of age at the pertussis episode.

Thus, there is an association between age of child at beginning of the pertussis episode and, if a pertussis disease, the risk of also suffering at least one complication due to the disease. The incidence rates of any complication were higher for children in the Göteborg study area in all age groups, but, given the pertussis disease, more children outside the Göteborg study area also had a complication during the pertussis episode.

2.8.2 Any complication, age and vaccination status at the pertussis episode

The event "any complication" was also studied in relation to age as well as vaccination status at beginning of the episode. Detailed data for children from the Göteborg study area are given in Table 19. The corresponding proportions for the 1 121 children outside the Göteborg study area (data not shown in table) were nearly the same as was reported in the main ten-year report (Table 12) for 2 035 children outside the Göteborg study area. The figures that we refer to in the text that follow concern the 1 121 children.

Table 19 Any complication due to the pertussis disease among children from the Göteborg study area born from January 1, 1996 until December 31, 2007, and surveyed from January 1, 2003 until December 31, 2007, by age at onset of cough and number of doses of a pertussis vaccine prior to the pertussis episode.

No of doses of a pertussis vaccine prior to the episode			Age of child at beginning of the pertussis episode							Total no. of children
			0-30 days	31-60 days	61-90 days	91-150 days	151-180 days	181-365 days	366- days	
Unimmunised children	**Any complication**	**No**	13	19	21	5	0	1	13	**72**
		Yes	3	10	5	2	0	1	3	**24**
	Total no. of children		**16**	**29**	**26**	**7**	**0**	**2**	**16**	**96**
	Rate of children with any complication		***19%***	***34%***	***19%***	***29%***	***0%***	***50%***	***19%***	***25%***
Children vaccinated with one dose	**Any complication**	**No**	-	-	-	29	10	3	1	**43**
		Yes	-	-	-	5	0	1	2	**8**
	Total no. of children		-	-	-	**34**	**10**	**4**	**3**	**51**
	Rate of children with any complication		-	-	-	***15%***	***0%***	***25%***	***67%***	***16%***
Children vaccinated with two or more doses	**Any complication**	**No**	-	-	-	-	4	65	336	**405**
		Yes	-	-	-	-	0	4	24	**28**
	Total no. of children		-	-	-	-	**4**	**69**	**360**	**433**
	Rate of children with any complication		-	-	-	-	***0%***	***6%***	***7%***	***6%***
All children regardless of vaccination status	**Any complication**	**No**	13	19	21	34	14	69	350	**520**
		Yes	3	10	5	7	0	6	29	**60**
	Total no. of children		**16**	**29**	**26**	**41**	**14**	**75**	**379**	**580**
	Rate of children with any complication		***19%***	***34%***	***19%***	***17%***	***0%***	***8%***	***8%***	***10%***

The overall rate of any complication for unvaccinated Göteborg study area children was 25%. The corresponding figure for children from the rest of Sweden was significantly higher 35%. For unimmunised children from the Göteborg study area aged 0-30, 31-60 and 61-90 days at the beginning of the pertussis episode the complication rate was 19%, 34% and 19%. Since there are very few children in each age groups from 3 months of age these age-groups were combined. For children older than 3 months of age the rate of any complication was 24%.

The corresponding complication rates for children outside the Göteborg study area were; 58%, 43%, 38% and 13% in the four age groups mentioned above – only for the youngest the observed difference was statistically significant. This downward trend of complication rate by increasing age are not observed for the vaccinated children, neither for children vaccinated with only one dose nor for children who have received two or more doses of a pertussis vaccine before the pertussis episode. Regardless of age the rate of any complication for children from the Göteborg study area vaccinated with one dose was 16%, and 6% for children vaccinated with 2 or more doses before the pertussis episode. For children from the rest of Sweden the corresponding figures were 27% respectively 10%.

Finally (and for obvious reasons), there was also a strong association between any complication and a hospital stay during the pertussis episode. Sixty-four percent, 180 of 280, of children with at least one complication also had a hospital admission due to the disease during the episode. For 1 421 children without any complication the hospitalisation rate was 9.6% ($p<0.001$). For children with any complication 47% of the hospital admissions had a duration 8 days or longer. For children without any complication 24% of the hospital admissions were longer than 8 days ($p<0.001$).

Again the figures for children from the Göteborg study area were quite different from those for Sweden except Göteborg. For children with any complication, 38% in the Göteborg study area and 71% in the rest of Sweden also had a hospital admission during the pertussis episode. For children without any complication the figures were 3.5% and 13.1% in the two areas. Both observed differences of hospitalisation rates between the two areas were statistically significant.

2.9 Spasmodic cough during the pertussis episode

Data on cough and spasmodic cough were available for all 1 705 children born January 1, 1996 until December 31, 2007 with a pertussis episode from January 1, 2003 until December 31, 2007. All children but 11 were coughing during their pertussis episode. One thousand three hundred and fifty-three (79.4%) had spasmodic cough during the pertussis episode and 352 (20.6%) reported no spasmodic cough.

2.9.1 Spasmodic cough for 21 or more days and age at the pertussis episode

Table 20 Number of pertussis cases with spasmodic cough for 21 days or more/Total number of episodes and percent with cough for 21 days or more by age at onset of cough among children born from January 1, 1996 until December 31, 2007, during surveillance from January 1, 2003 until December 31, 2007.

Spasmodic cough for 21 or more days	0 - < 3 months		3 - <5 months		5 -<12 months		≥12 months		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%
Sweden excluding Gbg area	236/265	89	112/125	90	57/74	77	522/659	79	927/1123	83
Göteborg study area	41/71	58	18/41	44	33/90	37	234/380	62	326/582	56
Total	277/336	82	130/166	78	90/164	55	756/1039	73	1253/1705	73

One thousand two hundred and fifty-three (73.5%) of the children had spasmodic cough for 21 or more days during the pertussis episode. The figures for a long duration of spasmodic cough were 326 (56.0%) for children in the Göteborg study area compared to 927 (82.5%) for children in the rest of the country, this difference was statistically significant. There were also significantly fewer cases with spasmodic cough for 21 or more days reported for Göteborg study area children in all age-groups (Table 20).

Age specific incidence rates of spasmodic cough for 21 days or longer due to pertussis per 100 000 years of follow up in the four age groups are shown in Figure 5 (solid lines), and age specific incidence rates for all pertussis (dotted lines).

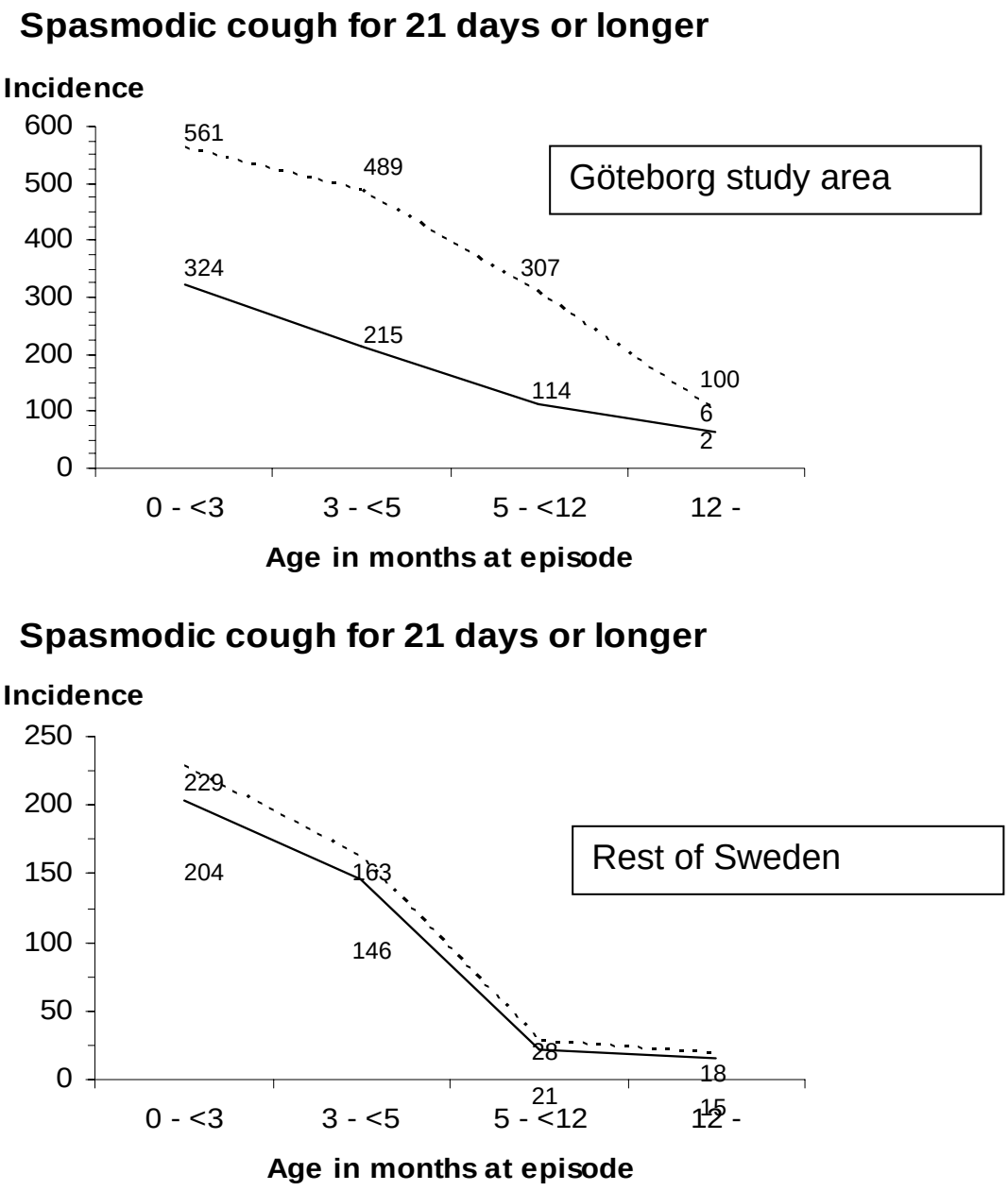

Figure 5 Age specific incidence of spasmodic cough for 21 or more days due to the pertussis disease, solid lines, and age specific incidence of all pertussis, dotted lines, per 100 000 years of follow-up regardless of vaccination status for children born from January 1, 1996 until December 31, 2007 with a laboratory confirmed *B. pertussis* reported from January 1, 2003 until December 31, 2007 for children in the Göteborg study area (upper diagram) and children in the rest of Sweden (lower diagram).

There was a "weak" association between age of child at beginning of the pertussis episode and the risk of also suffering a long duration of spasmodic cough during the pertussis disease. The risk for a long duration of spasmodic cough was high also for the elderly children.

2.9.2 Duration of spasmodic cough, age and vaccination status at the pertussis episode

Duration of spasmodic cough was also studied in relation to age as well as vaccination status at start of the pertussis episode. Detailed data are given in Table 21 for children from the Göteborg study area. Detailed data for children outside the Göteborg study area were presented in the main ten-year report (Table 13) – see discussion in section 2.6.2. The figures in the text that follow concern the 1 123 children in this report.

Table 21 Duration of spasmodic cough due to the pertussis disease among children born from January 1, 1996 until December 31, 2007, during surveillance from January 1, 2003 until December 31, 2007, by age at onset of cough and number of doses of a pertussis vaccine prior to the pertussis episode for children from the Göteborg study area.

Number of doses of a pertussis vaccine prior to the episode			Age of child at beginning of the pertussis episode							Total no. of children
			0-30 days	31-60 days	61-90 days	91-150 days	151-180 days	181-365 days	366- days	
Unimmunised children	**Duration of spasmodic cough**	**0 days**	7	6	10	3	0	0	2	**28**
		1-20 days	2	4	1	2	0	0	0	**9**
		21- days	7	19	15	2	0	2	14	**59**
	Total number of children		**16**	**29**	**26**	**7**	**0**	**2**	**16**	**96**
	Rate of children with spasmodic cough for 21 days or longer		***44%***	***66%***	***58%***	***29%***	***0%***	***100%***	***88%***	***61%***
Children vaccinated with one dose	**Duration of spasmodic cough**	**0 days**	-	-	-	14	1	1	1	**17**
		1-20 days	-	-	-	4	4	0	0	**8**
		21- days	-	-	-	16	5	3	2	**26**
	Total number of children		-	-	-	**34**	**10**	**4**	**3**	**51**
	Rate of children with spasmodic cough for 21 days or longer		-	-	-	***47%***	***50%***	***75%***	***67%***	***51%***
Children vaccinated with two or more doses	**Duration of spasmodic cough**	**0 days**	-	-	-	-	3	30	121	**154**
		1-20 days	-	-	-	-	1	17	22	**40**
		21- days	-	-	-	-	0	23	218	**241**
	Total number of children		-	-	-	-	**4**	**70**	**361**	**435**
	Rate of children with spasmodic cough for 21 days or longer		-	-	-	-	***0%***	***33%***	***60%***	***55%***
All children regardless of vaccination status	**Duration of spasmodic cough**	**0 days**	7	6	10	17	4	31	124	**199**
		1-20 days	2	4	1	6	5	17	22	**57**
		21- days	7	19	15	18	5	28	234	**326**
	Total number of children		**16**	**29**	**26**	**41**	**14**	**76**	**380**	**582**
	Rate of children with spasmodic cough for 21 days or longer		***44%***	***66%***	***58%***	***44%***	***36%***	***37%***	***62%***	***56%***

The overall rate of children with 21 or more days of spasmodic cough for unvaccinated children from the Göteborg study area was 61%. The corresponding figure for children from the rest of Sweden was significantly higher 91%.

For unvaccinated children from the Göteborg study area aged 0-30, 31-60 and 61-90 days at the beginning of the pertussis episode the rate was 44%, 66% and 58% respectively. Since there are very few children in each age group from 3 months of age they are combined and for children older than 3 months of age the rate was 72%. The corresponding rates for children outside the Göteborg study area were all significantly higher; 90%, 90%, 88% and 94% in the four age groups mentioned above.

Regardless of age the rate of children with 21 or more days of spasmodic cough among vaccinated with one dose was 51% and among those vaccinated with 2 or more doses 55% for children from the Göteborg study area and significantly higher, 88% respectively 76%, for children from the rest of Sweden.

2.10 Duration of cough and antibiotic treatment

As stated in section 2.9, data on cough and spasmodic cough were available for all 1 705 children born from January 1, 1996 until December 31, 2007 and under surveillance from January 1, 2003 until December 31 ,2007, whereof 666 were infants. All children but 11 were coughing during their pertussis episode, including 2 infants.

Applying the EU clinical case definition of pertussis with 2 weeks of more of coughing (any type) in conjunction with positive laboratory sample, in all 1 639/1 705 (96.1%) would fulfil this definition. Among the 66 cases that would not fulfil the EU definition, 27 were infants and 39 were children one year or older. All but three infants had received erythromycin or trimetoprim-sulfametoxazol, whereas seven of the 39 children were not treated with antibiotics. Fourteen of those infants were unvaccinated, 5 had received one dose and 8 had received two doses. All 39 children had received three doses.

2.10.1 Duration of cough, spasmodic cough and antibiotic treatment

There was information on antibiotic treatment, or not, including date at start of treatment for 1 702 of 1 705 episodes, including 665 of 666 infants. No treatment at all was reported for 615 of the episodes, whereof 74 were episodes for infants. Before further statistical analysis 18 treated cases with a short erythromycin treatment, 1 – 6 days, were first excluded. Most often the described treatment period was shortened due to diarrhoea etc.

Table 22 presents 1 479 children, whereof 526 were from the Göteborg study area and 953 from Sweden except the Göteborg study area. There were 331 children aged 0-90 days at onset of the episode, without any pertussis vaccination prior to onset, 127 children aged 91-150 days at onset of the episode, with one dose of a pertussis vaccine prior to onset, 115 children aged 151-365 days at onset of the episode, with two doses of a pertussis vaccine prior to onset, and 906 children one year or older at onset of the episode, with three or more doses prior to onset.

Children below one year of age were in general treated with antibiotics. In the Göteborg study area 159/176 (90.3%) of infants were treated, in the rest of Sweden 350/397 (88.2%). The proportions treated were highest in the youngest, i.e. those below 3 months of age, with 64/70 (91.4 %), treated in the Göteborg study area and 239/261 (91.6%) in the rest of Sweden. The proportion of infants treated remained high in the Göteborg area also for the age-group 3 to below 5 months (33/34, i.e. 97.1 %) but there was a slight decrease in the rest of Sweden (75/93, i.e. 80.6 %). From 5 to below 12 months the proportion treated in Göteborg was 62/72 (86.1%) and 36/43 (83.7%) in the rest of Sweden. Among those aged one year or more at onset of cough during the episode, 181/350 (51.7%) of Göteborg study area children were treated and so were 261/556 (46.9%) of the children from the rest of Sweden.

Table 22 Duration of cough and spasmodic cough due to the pertussis disease among children born from January 1, 1996 until December 31, 2007 and under surveillance from January 1, 2003 until December 31, 2007, by age at onset of cough and start of antibiotic treatment in relation to onset of the pertussis episode.

Age at beginning of episode	Day after onset of cough for start of antibiotic treatment with Erytromycin etc. during the pertussis episode	Area								
		Göteborg study area			Sweden except Göteborg			Sweden		
		Duration, days of cough		Duration, days of spasmodic cough	Duration, days of cough		Duration, days of spasmodic cough	Duration, days of cough		Duration, days of spasmodic cough
		N	Median	Median	N	Median	Median	N	Median	Median
0-90 days	**No treatment**	6	30.5	9.5	22	48	34.5	28	45	32
	Start day ≤6	***21***	***26***	***0***	***31***	***44***	***42***	***52***	***38.5***	***30.5***
	Start day 7-13	20	45	30.5	79	45	35	99	45	35
	Start day ≥ 14	23	45	32	129	48	37	152	47.5	37
	Total	70	39.5	25.5	261	47	37	331	45	35
91-150 days	**No treatment**	1	164	96	18	49.5	40	19	51	41
	Start day ≤6	***11***	***22***	***0***	***6***	***32***	***25.5***	***17***	***24***	***16***
	Start day 7-13	12	41	6.5	25	40	34	37	40	32
	Start day ≥ 14	10	46.5	39	44	51.5	42.5	54	49	42
	Total	34	41.5	17	93	47	39	127	46	36
151-365 days	**No treatment**	10	32.5	0	7	52	26	17	34	0
	Start day ≤6	***10***	***13.5***	***3.5***	***5***	***33***	***0***	***15***	***19***	***0***
	Start day 7-13	25	30	11	12	43	34.5	37	32	23
	Start day ≥ 14	27	33	14	19	45	35	46	39	23
	Total	72	30.5	8.5	43	45	31	115	33	17
1 year or older	**No treatment**	169	48	30	295	49	34	464	49	32
	Start day ≤6	***38***	***13.5***	***0***	***26***	***26.5***	***6.5***	***64***	***15***	***0***
	Start day 7-13	47	32	16	73	41	32	120	38	28
	Start day ≥ 14	96	49.5	32	162	55.5	41	258	53	37
	Total	350	43	26.5	556	49	35	906	47	32
All ages	**No treatment**	186	46.5	28.5	342	49	34.5	528	48	32
	Start day ≤6	***80***	***15***	***0***	***68***	***36.5***	***31***	***148***	***25.5***	***9***
	Start day 7-13	104	32	19.5	189	43	34	293	40	30
	Start day ≥ 14	56	46	31	354	51	38	510	49	36
	Total	526	40	24	953	48	36	1479	46	32

An early start of the antibiotic treatment, within the first week (<=6 days) after onset of cough during the episode was, in all age groups and for each area, associated with a shorter duration of cough compared to both "no antibiotic treatment" and a late start, later than two weeks after onset. The same was true, with some exceptions, for spasmodic cough.

3 Additional analyses from the Göteborg study area

3.1 Material and methods

3.1.1 Background, the surveillance database

See also Section 2.1.1 and 2.1.2. In order to also cover the first 5 ¼ Göteborg years, i.e. the period not included in the enhanced follow-up for children from this area of Sweden, we have in a separate nine year report [5] made two additional types of analyses, previously not done within the surveillance project, with the present report updating these analyses until December 31, 2007.

The first is to use the common information we collected for all children in Sweden in the inclusion process of the enhanced surveillance, i.e. the birth date of the child and the date for the laboratory-confirmed pertussis sample. Thus, all routine reports of laboratory-confirmed pertussis occurring in the Göteborg study area from September 1, 1997 through December 31, 2002, were also entered in the surveillance database but without any clinical follow-up or vaccination data. We have calculated age at sampling date for these reports, and also for all other reports of laboratory-confirmed pertussis including those followed-up within the enhanced surveillance. By doing this, we can compare ten years of age-specific data from the Göteborg study area and from the rest of Sweden, although without clinical and vaccination data. This is performed in Sections 3.3-3.4.

The second additional type of analyses include a retrospective collection of missing vaccination data from the first 5 ¼ year of culture- or PCR-confirmed reports from the Göteborg study area. This was in autumn 2006 done by telephoning the Child or School Health Care nurses with access to the individual medical record. By combining vaccination data with age at date of sampling, we have estimated age-specific incidence in children vaccinated with at least two doses prior to the date for sampling for the whole ten year period, thereby allowing a comparison between the Göteborg study area and the rest of Sweden for the whole surveillance period for children with known vaccination status. This part is reported in Sections 3.5-3.7.

3.1.2 Person time and incidence calculations

See section 2.1.4

3.1.3 Göteborg study area, vaccines and vaccinated cohorts

See section 2.2

3.2 Pertussis reports used for the 10 year additional analyses

In the beginning of March 2008 there were 1 382 episodes reported in the surveillance database from children in the Göteborg study area, whereof 1 237 occurred from October 1, 1997 until December 31, 2007 among children born from January 1, 1996 until December 31, 2007. From other parts of Sweden there were 2 148 episodes reported in the surveillance database for the same birth period and the same calendar period. (In the main 10 y report 106 of those episodes were not included since they lacked clinical follow-up data.) In Sections 3.3-3.4, we use all these 3 385 reports (1 237 from Göteborg study area and 2 148 from the rest of Sweden) for comparison of pertussis incidence in different age-groups between children in the Göteborg study area and in the rest of Sweden. The approach in Tables 25-27 is an intent to treat, i.e. the overall effect of the vaccination program.

From November 2006 until April 2007 we performed a retrospective collection of individual vaccination history for 621 culture- or PCR-confirmed cases of pertussis occurring during the 5 ¼ year period when the Göteborg study area was not included in the enhanced surveillance, i.e. from October 1, 1997 and until December 31, 2002. The individual vaccination history was collected for all but 7 of the 621 cases. In summary, information on vaccination status at date for the positive sample exists for 1 200 (97.0%) of the 1 237 episodes for children from the Göteborg area, and for 2 115 (98.5%) of the 2 148 episodes for children from other parts of Sweden. In Sections 3.5-3.7, we use these 3 315 reports (1 200 from

Göteborg study area and 2 115 from the rest of Sweden) for comparison of pertussis incidence, for vaccinated children in different age-groups, between the Göteborg study area and the rest of Sweden. The incidence analyses in Tables 27-29 are done for children vaccinated with at least two doses prior to the laboratory report (the vaccine failures). The approach in these tables is more similar to a per protocol analyses, i.e. the tables indicate the effect of the vaccination program in children who are vaccinated according to the recommendations of this program.

3.3 Culture-confirmed pertussis per calendar period & birth cohort

In Table 23 all 3 385 culture- or PCR-reported cases from October 1, 1997 until December 31 ,2007, in children born from January 1, 1996 until December 31, 2007 are shown for the Göteborg study area and the rest of Sweden. In Table 24 results are given, for the same groups of children, but for age in one-year age groups and year of positive sample.

Table 23 Number of positive samples, per area, according to year of birth and year of positive sample.

Area			Year of laboratory positive sample											Total
			1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	
Göteborg study area	Year of birth	1996	3	3	7	21	9	23	7	37	4	6	0	**120**
		1997	2	7	7	17	12	15	8	38	15	2	1	**124**
		1998	-	12	27	40	26	23	2	46	10	4	0	**190**
		1999	-	-	27	65	24	21	8	40	10	4	3	**202**
		2000	-	-	-	34	30	33	6	13	4	1	1	**122**
		2001	-	-	-	-	32	53	10	29	6	1	0	**131**
		2002	-	-	-	-	-	49	20	32	5	0	4	**110**
		2003	-	-	-	-	-	-	28	59	11	2	2	**102**
		2004	-	-	-	-	-	-	-	74	18	1	2	**95**
		2005	-	-	-	-	-	-	-	-	11	9	0	**20**
		2006	-	-	-	-	-	-	-	-	-	10	5	**15**
		2007	-	-	-	-	-	-	-	-	-	-	6	**6**
	Total		**5**	**22**	**68**	**177**	**133**	**217**	**89**	**368**	**94**	**40**	**24**	**1237**
Sweden except Gbg	Year of birth	1996	5	17	39	45	19	40	19	59	47	14	3	**307**
		1997	22	32	19	24	17	32	7	27	26	14	18	**238**
		1998	-	54	45	16	7	17	12	32	42	23	16	**264**
		1999	-	-	94	72	12	20	9	18	24	15	19	**283**
		2000	-	-	-	89	34	16	7	20	16	22	19	**223**
		2001	-	-	-	-	32	23	9	16	14	10	9	**113**
		2002	-	-	-	-	-	103	21	18	11	8	4	**165**
		2003	-	-	-	-	-	-	49	48	10	7	7	**121**
		2004	-	-	-	-	-	-	-	121	46	14	7	**188**
		2005	-	-	-	-	-	-	-	-	80	18	5	**103**
		2006	-	-	-	-	-	-	-	-	-	68	25	**93**
		2007	-	-	-	-	-	-	-	-	-	-	50	**50**
	Total		**27**	**103**	**197**	**246**	**121**	**251**	**133**	**359**	**316**	**213**	**182**	**2148**

Taken population sizes for the two areas into account, in mean 9.5% of the children were born in the Göteborg study area and 90.5% in the rest of Sweden, the number of cases for each birth-cohort (but 2007) and for each calendar year, are higher than expected for the Göteborg study area compared to the rest of Sweden.

Table 24 Number of positive samples, per area, according to year of age in one-year classes, and year of positive sample for children at date for the positive sample. Figures in italics indicate a transition period, i.e. only at about half of number of children of these age/year-groups were covered by the enhanced surveillance.

Area			Year of laboratory positive sample											Total
			1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	
Göteborg study area	Year of age	0	3	13	42	67	52	91	43	115	25	16	10	**477**
		1	***2***	7	15	57	19	31	9	38	11	4	1	**194**
		2	-	***2***	5	21	25	27	11	27	6	1	2	**127**
		3	-	-	***6***	22	18	19	2	16	7	1	1	**92**
		4	-	-	-	***10***	13	17	7	28	4	1	2	**82**
		5	-	-	-	-	***6***	22	3	41	6	1	3	**82**
		6	-	-	-	-	-	***10***	9	45	14	2	1	**81**
		7	-	-	-	-	-	-	***5***	40	12	4	3	**64**
		8	-	-	-	-	-	-	-	***18***	8	4	0	**30**
		9	-	-	-	-	-	-	-	-	***1***	1	0	**2**
		>=10	-	-	-	-	-	-	-	-	-	***5***	1	**6**
	Total		**5**	**22**	**68**	**177**	**133**	**217**	**89**	**368**	**94**	**40**	**24**	**1237**
Sweden except Gbg	Year of age	0	24	77	128	154	59	119	67	160	122	84	73	**1067**
		1	***3***	18	15	20	12	11	8	15	11	9	5	**127**
		2	-	***8***	29	16	11	24	8	22	6	12	5	**141**
		3	-	-	***25***	29	13	16	6	11	14	7	6	**127**
		4	-	-	-	***27***	16	27	12	20	15	8	8	**133**
		5	-	-	-	-	***10***	28	10	25	19	16	4	**112**
		6	-	-	-	-	-	***26***	16	27	28	18	19	**134**
		7	-	-	-	-	-	-	***6***	42	37	20	18	**123**
		8	-	-	-	-	-	-	-	***37***	32	18	13	**100**
		9	-	-	-	-	-	-	-	-	***32***	15	20	**67**
		>=10	-	-	-	-	-	-	-	-	-	***6***	11	**17**
	Total		**27**	**103**	**197**	**246**	**121**	**251**	**133**	**359**	**316**	**213**	**182**	**2148**

3.4 Person-time of follow-up, incidence and relative risk calculations

In Table 25, total person-time of follow-up, number of observed culture- or PCR-confirmed cases, incidence per 100 000 person years and relative risk are calculated, irrespective of vaccination status, for different age-groups for children born from January 1, 1996 until December 31, 2007, for pertussis episodes which occurred from October 1, 1997 until December 31, 2007 in two areas of Sweden – Sweden except Gbg, and the Göteborg study area.

In Tables 26 and 27 the corresponding comparisons are performed for two birth periods; children born 1996–1998, and children born 2000 or later. For children from the Göteborg study area the first birth period means children in a nearly pure DiTeKik® cohort, while in the second birth period most children in this area have received Pentavac®, (except for children in Kungsbacka, approximately 5%, who received either Infanrix®-Polio-Hib or Pentavac®). The children born 1999 are not included in these tables because they represent a transition cohort with mixed vaccinations within the 3-5-12 month schedule. As for Table 25 vaccination status is not used in these two tables.

Table 25 Children born **from January 1, 1996 until December 31, 2007**, and followed from **October 1, 1997 until December 31, 2007** with observed Culture- or PRC-confirmed *B.pertussis.* We present Person-years of follow-up, Number of laboratory confirmed cases, Incidence per 100 000 person-years of follow-up and Relative risk of having a laboratory-verified episode of *B.pertussis* (for children in Sweden except the Göteborg study area compared to children in this area) in the following age-groups at the pertussis episode; 0-<3 months of age; 3-<5 months of age; 5-<12 months of age; and after12 months of age in ten age intervals. Age is calculated at the date of the positive sample.

Date of positive sample occurred	Person-years of follow-up	Number of laboratory confirmed cases	Incidence per 100 000 person-years and 95% confidence interval	Relative risk Göteborg compared to Sweden except Gbg
During 0 - <3 months of age				
Sweden except Gbg	223 435	455	203 (185-223)	-
Göteborg study area	*24 045*	*146*	*607 (512-711)*	***3.0 (2.5 – 3.6)***
During 3 - <5 months of age	-	-	-	-
Sweden except Gbg	148 460	357	240 (216-267)	-
Göteborg study area	*15 950*	*99*	*621 (505-755)*	***2.6 (2.1 – 3.2)***
During 5 - <12 months of age	-	-	-	-
Sweden except Gbg	516 635	255	49 (43-56)	-
Göteborg study area	*55 330*	*232*	*419 (367-475)*	***8.5 (7.1 – 10.2)***
During 1 year of age	-	-	-	-
Sweden except Gbg	875 275	127	15 (12-17)	-
Göteborg study area	*93 050*	*194*	*209 (179-240)*	***14.4 (11.5 – 18.0)***
During 2 years of age	-	-	-	-
Sweden except Gbg	806 285	141	17 (15-21)	-
Göteborg study area	*85 205*	*127*	*149 (123-175)*	***8.5 (6.7 – 10.8)***
During 3 years of age	-	-	-	-
Sweden except Gbg	715 130	127	18 (15-21)	-
Göteborg study area	*75 215*	*92*	*122 (98-150)*	***6.9 (5.3 – 9.0)***
During 4 years of age	-	-	-	-
Sweden except Gbg	624 815	133	21 (18-25)	-
Göteborg study area	*65 490*	*82*	*125 (100-155)*	***5.9 (4.5 – 7.8)***
During 5 years of age	-	-	-	-
Sweden except Gbg	536 690	112	21 (17-25)	-
Göteborg study area	*56 125*	*82*	*146 (116-181)*	***7.0 (5.3 – 9.3)***
During 6 years of age	-	-	-	-
Sweden except Gbg	452 115	134	30 (25-35)	-
Göteborg study area	*47 050*	*81*	*172 (137-214)*	***5.8 (4.4 – 7.7)***
During 7 years of age	-	-	-	-
Sweden except Gbg	369 930	123	33 (28-39)	-
Göteborg study area	*38 285*	*64*	*167 (129-213)*	***5.0 (3.7 – 6.8)***
During 8 years of age	-	-	-	-
Sweden except Gbg	289 120	100	35 (28-42)	-
Göteborg study area	*29 790*	*30*	*101 (68-144)*	***2.9 (1.9 – 4.4)***
During 9 years of age	-	-	-	**-**
Sweden except Gbg	208 930	67	32 (25-41)	**-**
Göteborg study area	*21 380*	*2*	*9 (1-34)*	***0.3 (0.1 – 1.2)***
During 10 or 11 years of age	-	-	-	**-**
Sweden except Gbg	170 885	17	10 (6-16)	**-**
Göteborg study area	*17 330*	*6*	*35 (13-76)*	***3.5 (1.4 – 8.8)***
During 1 year of age or later	-	-	-	**-**
Sweden except Gbg	5 049 175	1081	21 (20-23)	**-**
Göteborg study area	*528 920*	*760*	*144 (134-154)*	***6.7 (6.1 – 7.4)***

Table 26 Children born from **January 1, 1996 until December 31, 1998**, and followed from **October 1, 1997 until December 31, 2007,** with observed Culture- or PRC-confirmed *B.pertussis.* We present Person-years of follow-up, Number of laboratory confirmed cases, Incidence per 100 000 person-years of follow-up and Relative risk of having a laboratory-verified episode of *B.pertussis* (for children in Sweden except Gbg (except the Göteborg study area) compared to children in the Göteborg study area). Age is calculated at the date of the positive sample.

Date of positive sample occurred	Person-years of follow-up	Number of laboratory confirmed cases	Incidence per 100 000 person years and 95% confidence interval	Relative risk Göteborg study area compared to Sweden except Gbg	
During 0 - <3 months of age					
Sweden except Gbg	27 840	38	136 (97-188)		
Göteborg study area	*2 905*	*5*	*172 (56-403)*	***1.3***	***(0.5 – 3.2)***
During 3 - <5 months of age	-	-	-		**-**
Sweden except Gbg	21 410	42	196 (142-265)		**-**
Göteborg study area	*2 225*	*7*	*314 (126-647)*	***1.6***	***(0.7 – 3.6)***
During 5 - <12 months of age	-	-	-		**-**
Sweden except Gbg	93 035	55	59 (44-76)		**-**
Göteborg study area	*9 640*	*19*	*197 (118-308)*	***3.3***	***(2.0 – 5.6)***
During 1 year of age	-	-	-		**-**
Sweden except Gbg	224 875	49	22 (16-29)		**-**
Göteborg study area	*23 155*	*49*	*212 (157-280)*	***9.7***	***(6.5 – 14.4)***
During 2 years of age	-	-	-		**-**
Sweden except Gbg	249 215	57	23 (17-30)		**-**
Göteborg study area	*25 605*	*38*	*148 (105-204)*	***6.5***	***(4.3 – 9.8)***
During 3 years of age	-	-	-		**-**
Sweden except Gbg	249 215	75	30 (24-38)		**-**
Göteborg study area	*25 605*	*58*	*227 (172-293)*	***7.5***	***(5.3 – 10.6)***
During 4 years of age	-	-	-		**-**
Sweden except Gbg	249 215	76	30 (24-38)		**-**
Göteborg study area	*25 605*	*40*	*156 (112-213)*	***5.1***	***(3.5 – 7.5)***
During 5 years of age	-	-	-		**-**
Sweden except Gbg	249 215	60	24 (18-31)		**-**
Göteborg study area	*25 605*	*49*	*191 (142-253)*	***8.0***	***(5.5 – 11.6)***
During 6 years of age	-	-	-		**-**
Sweden except Gbg	249 215	83	33 (26-41)		**-**
Göteborg study area	*25 605*	*72*	*281 (220-354)*	***8.4***	***(6.2 – 11.6)***
During 7 years of age	-	-	-		**-**
Sweden except Gbg	249 215	97	39 (31-47)		**-**
Göteborg study area	*25 605*	*59*	*230 (175-297)*	***5.9***	***(4.3 – 8.2)***
During 8 years of age	-	-	-		**-**
Sweden except Gbg	249 215	93	37 (30-46)		
Göteborg study area	*25 605*	*30*	*117 (79-167)*	***3.1***	***(2.1 – 4.7)***
During 9 years of age	-	-	-		**-**
Sweden except Gbg	208 930	67	32 (25-41)		
Göteborg study area	*21 380*	*2*	*9 (1-34)*	***0.3***	***(0.1 – 1.2)***
During 10 or 11 years of age	-	-	-		**-**
Sweden except Gbg	170 885	17	10 (6-16)		
Göteborg study area	*17 330*	*6*	*35 (13-76)*	***3.5***	***(1.4 – 8.8)***
During 1 year of age or later	-	-	-		**-**
Sweden except Gbg	2 349 195	674	29 (27-31)		
Göteborg study area	*241 100*	*403*	*167 (151-184)*	***5.8***	***(5.2 – 6.6)***

Table 27 Children born from **January 1, 2000 until December 31, 2007**, and followed from **January 1, 2000 until December 31, 2007** with observed Culture- or PRC-confirmed *B.pertussis*. We present Person-years of follow-up, Number of laboratory confirmed cases, Incidence per 100 000 person-years of follow-up and Relative risk of having a laboratory-verified episode of *B.pertussis* (for children in Sweden except Gbg (except the Göteborg study area) compared to children in the Göteborg study area) in the following age-groups at the pertussis episode; 0-<3 months of age; 3-<5 months of age; 5-<12 months of age; and after12 months of age in six age intervals. Age is calculated at the date of the positive sample.

Date of positive sample occurred	Person-years of follow-up	Number of laboratory confirmed cases	Incidence per 100 000 person years and 95% confidence interval	Relative risk Göteborg study area compared to Sweden except Gbg
During 0 - <3 months of age	-	-	-	-
Sweden except Gbg	175 645	364	207 (186-229)	-
Göteborg study area	*19 050*	*132*	*693 (577-819)*	***3.3 (2.7 – 4.1)***
During 3 - <5 months of age	-	-	-	-
Sweden except Gbg	113 750	263	231 (204-260)	-
Göteborg study area	*12 330*	*78*	*633 (500-789)*	***2.7 (2.1 – 3.5)***
During 5 - <12 months of age	-	-	-	-
Sweden except Gbg	377 045	146	39 (33-46)	-
Göteborg study area	*40 810*	*176*	*431 (370-497)*	***11.2 (9.0 – 13.9)***
During 1 year of age	-	-	-	-
Sweden except Gbg	570 590	66	12 (9-15)	-
Göteborg study area	*61 540*	*104*	*169 (138-203)*	***14.6 (11.0 – 19.4)***
During 2 years of age	-	-	-	-
Sweden except Gbg	477 260	65	14 (11-17)	-
Göteborg study area	*51 235*	*60*	*117 (89-151)*	***8.6 (6.1 – 15.0)***
During 3 years of age	-	-	-	-
Sweden except Gbg	386 105	41	11 (8-14)	
Göteborg study area	*41 245*	*26*	*63 (41-92)*	***5.9 (3.6 – 9.7)***
During 4 years of age	-	-	-	-
Sweden except Gbg	295 790	46	16 (11-21)	
Göteborg study area	*31 520*	*18*	*57 (34-90)*	***3.7 (2.1 – 6.3)***
During 5 years of age	-	-	-	-
Sweden except Gbg	207 665	29	14 (9-20)	
Göteborg study area	*22 150*	*6*	*27 (22-59)*	***1.9 (0.8 – 4.7)***
During 6 or 7 years of age	-	-	-	-
Sweden except Gbg	163 990	36	22 (15-30)	
Göteborg study area	*17 395*	*1*	*6 (0-32)*	***0.3 (0.1 – 1.9)***
During 1 year of age or later	-	-	-	-
Sweden except Gbg	2 101 400	283	13 (12-15)	
Göteborg study area	*225 085*	*215*	*96 (83-109)*	***7.1 (5.9 – 8.5)***

3.4.1 Comments to incidence and risk tables

Also in this larger group (Table 25), the number of cases reported from Göteborg was high in relation to population size in the area, with 477 reported infant cases and 760 cases in children aged 1 year or more. From the rest of Sweden there were 1 067 infant cases and 1 081 cases in children aged from 1 year.

For children born from January 1, 1996 until December 31, 1998 (Table 26), in each age-group from 5-<12 months until 8 years of age there was a statistically significant higher risk (RR=3.1 – RR=9.7) of receiving pertussis for children in the Göteborg study area compared to children in the rest of the country. From 12 months of age the relative risk was 5.8 (95% C.I. 5.2 – 6.6) and the incidence figures per 100 000

years of follow-up was 167 for children in the Göteborg study area and 29 for children living outside that area.

Corresponding Table 27 presents result for 601 and 1 056 children born January 1, 2000 until December 31, 2007 with a laboratory confirmed pertussis for children living in the Göteborg study area respectively in Sweden except Göteborg. In each age group until 4 years of age there was a statistically significant higher risk (RR=2.7 – RR=14.6) of receiving pertussis for children in the Göteborg study area compared to children in the rest of the country. From 12 months of age the relative risk was 7.1 (95% C.I. 5.9 – 8.5) and the incidence figures per 100 000 years of follow-up was 96 for children in the Göteborg study area and 13 for children living outside that area.

3.5 Vaccination history at date of positive laboratory sample

For comparison of pertussis incidence for vaccinated children between the Göteborg study area and the rest of Sweden, we use reports of culture- or PCR-confirmed pertussis from October 1, 1997 until December 31, 2007 among children born from January 1, 1996 until December 31, 2007 from children for whom we have access to vaccination history at date for the positive sample – in total 1 200 reports from Göteborg study area and 2 115 from the rest of Sweden. Eight hundred and seventy-two respectively 1 043 children in the two areas were vaccinated with at least two doses of a pertussis vaccine prior to the date of the laboratory-confirmed pertussis (Table 28).

Table 28 Vaccination history at date of the positive sample for children in Göteborg area and in Sweden except Göteborg, for children born January 1, 1996 until December 31, 2007 and for culture or PCR positive pertussis episodes from October 1, 1997 until December 31, 2007.

			Göteborg study area		Sweden except Gbg		Total
				Percent between area		Percent between area	
Number of doses before positive sample	Not vaccinated	Number of episodes	196	20,2	775	79,8	971
		Percent within area	*16,3*	-	*36,7*	-	*29,3*
	One dose	Number of episodes	132	30,8	297	69,2	429
		Percent within area	*11,0*	-	*14,0*	-	*12,9*
	Two doses	Number of episodes	195	56,2	152	43,8	347
		Percent within area	*16,3*	-	*7,2*	-	*10,5*
	Three or more doses	Number of episodes	677	43,2	891	56,8	1568
		Percent within area	*56,4*	-	*42,1*	-	*46,7*
Total		Number of episodes	1 200	36,2	2 115	63,8	3 315

Figures in Table 28 further confirm conclusion in section 2.4 that relatively more cases are reported among not vaccinated in Sweden except Göteborg (36.7% vs 16.3%) and, consequently, relatively more cases were reported among vaccinated in the Göteborg study area, specifically among those who had received at least two doses of a pertussis vaccine (72.7% vs 49.3%) before the date of the positive sample ("Percent within area"). Figures in column "Percent between area" (nearly "equal" to those of Table 2 in section 1.3.3), taking the follow-up time for children in the Göteborg study area (9.5% of the total amount of follow-up) into account, tell the same story. The "overrepresentation" of reported pertussis cases in children from the Göteborg study area varies between a multiple of 2.1 (for not vaccinated) and 5.9 (for those vaccinated with two doses).

Since data for the unvaccinated and for those vaccinated with only one dose prior to the date for the positive sample already are represented in the intent-to-treat incidence tables in section 3.4, Tables 25-27 and since tables for the slightly smaller data-set used in sections 3.5-3.7 (70 episodes fewer than used in section 3.4) should be nearly identical to those in Section 3.4, the age-specific incidence tables of section 3.7, will include only children vaccinated with two or more doses prior to the date of the positive sample. Thus, incidence tables in section 3.7 should be regarded as a complement to Section 3.4, Tables 25-27, (the intent-to treat analyses), and to Table 14 of the Section 2 analyses. The last mentioned table gives age-

specific incidence for a smaller data-set of episodes occurring from January 1, 2003 for children vaccinated with at least two doses of a pertussis vaccine prior to onset of cough. However, in section 3.6 some descriptive data, for episodes with less than two doses prior to the positive sample, are first presented.

3.6 Lab. confirmed pertussis in children born Jan. 1, 1996 until Dec. 31, 2007

For those birth cohorts of children there were 3 315 reports of laboratory confirmed pertussis from October 1, 1997 until December 31, 2007 for which we have data on vaccination status prior to the date of the positive sample, Table 29.

Table 29 Number of reported laboratory confirmed cases of pertussis from October 1, 1997 until December 31, 2007 per birth-cohort from January 1, 1996 until December 31, 2007, per number of pertussis vaccine doses prior to the positive sample and per area for the pertussis episode.

Birth-cohort	Number of doses of a pertussis vaccine	Sweden except Göteborg		Göteborg study area		Total
		Not vaccinated	Vaccinated	Not vaccinated	Vaccinated	
1996	0	28	-	4	-	32
	1	-	2	-	1	3
	2	-	5	-	4	9
	3	-	268	-	109	377
1997	0	39	-	3	-	42
	1	-	13	-	2	15
	2	-	20	-	4	24
	3	-	163	-	110	273
1998	0	58	-	12	-	70
	1	-	28	-	10	38
	2	-	22	-	17	39
	3	-	156	-	145	301
1999	0	109	-	18	-	127
	1	-	46	-	24	70
	2	-	27	-	30	57
	3	-	96	-	123	219
2000	0	100		19	-	119
	1	-	35	-	13	48
	2	-	10	-	22	32
	3	-	75	-	61	136
2001	0	39		23		62
	1	-	16	-	18	34
	2	-	10	-	32	42
	3	-	47	-	51	98
2002	0	88		32		120
	1	-	36	-	18	54
	2	-	5	-	16	21
	3	-	32	-	44	76
2003	0	57	-	24	-	81
	1	-	16	-	11	27
	2	-	18	-	40	58
	3	-	28	-	24	52
2004	0	94	-	40	-	134
	1	-	54	-	27	81
	2	-	20	-	21	41
	3	-	20	-	7	27
2005	0	66	-	8	-	74
	1	-	18	-	3	21
	2	-	6	-	6	12
	3	-	5	-	3	8
2006	0	59	-	10	-	69

	1	**-**	**22**	**-**	**3**	**25**
	2	**-**	**9**	**-**	**2**	**11**
	3	**-**	**1**	**-**	**0**	**1**
2007	**0**	**38**	**-**	**3**	**-**	**41**
	1	**-**	**11**	**-**	**2**	**13**
	2	**-**	**0**	**-**	**1**	**1**
	3	**-**	**0**	**-**	**0**	**0**
Total	**0**	**775**	**-**	**196**	**-**	**971**
Total	**1**	**-**	**297**	**-**	**132**	**429**
Total	**2**	**-**	**152**	**-**	**195**	**347**
Total	**3**	**-**	**891**	**-**	**677**	**1 568**
Total	**0 – 3**	**775**	**1 340**	**196**	**1 004**	**3 315**

Since we lack proper information of onset of the pertussis episode, i.e. a date for onset of cough for many of the reports, we use the date for the positive sample (available for all reports) as a proxy. Thus, in the Part 3 analyses we calculate the age at "onset" of episode as the difference between that date and the date of birth. From the enhanced surveillance reports we know that onset of cough generally occurs one to two weeks before the sample was taken.

Table 30 shows the age distribution, at date of the positive sample, for unvaccinated children and for children with one dose prior to that date. Age groups are the same as in Table 25.

Table 30 Number of reported laboratory confirmed cases of pertussis from October 1, 1997 until December 31, 2007 per birth-cohort from January 1, 1996 until December 31, 2007, for unvaccinated and for children vaccinated with one dose prior to the date of the positive sample per age-group and per area for the pertussis episode.

Date of positive sample occurred in age-interval	**Sweden except Göteborg**				**Göteborg study area**			
	Not vaccinated		**Vaccinated with one dose**		**Not vaccinated**		**Vaccinated with one dose**	
	No.	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**
During 0-<3 months	**448**	**57,8**	**0**		**142**	**72,4**	**0**	
During 3-<5 months	**138**	**17,8**	**210**	**70,7**	**22**	**11,2**	**73**	**55,3**
During 5-<12 months	**39**	**5,0**	**81**	**27,3**	**3**	**1,5**	**51**	**38,6**
During 1 year	**34**	**4,4**	**1**	**0,3**	**4**	**2,0**	**2**	**1,5**
During 2 years	**23**	**3,0**	**0**		**5**	**2,6**	**1**	**0,8**
During 3 years	**19**	**2,5**	**2**	**0,7**	**3**	**1,5**	**0**	
During 4 years	**24**	**3,1**	**2**	**0,7**	**5**	**2,6**	**0**	
During 5 years	**16**	**2,1**	**0**		**5**	**2,6**	**1**	**0,8**
During 6 years	**10**	**1,3**	**0**		**6**	**3,1**	**3**	**2,3**
During 7 years	**12**	**1,5**	**0**		**0**		**1**	**0,8**
During 8 years	**8**	**1,0**	**1**	**0,3**	**1**	**0,5**	**0**	
During 9 years	**3**	**0,4**	**0**		**0**		**0**	
During 10-11 years	**1**	**0,1**	**0**		**0**		**0**	
Total	**775**		**297**		**196**		**132**	

Most of the pertussis case among unvaccinated children occurred, as expected, in the two youngest age-groups – 75.6% and 83.6% in Sweden except Göteborg respectively in the Göteborg study area. In Sweden except Göteborg 150 cases (19.4%) occurred, with a date for the positive sample, after one year of age. In the Göteborg study area there were 29 cases (14.8%) older than one year.

For vaccinated with only one dose prior to the date of the positive sample very few cases occurred after one year of age and the majority of the one-dose vaccinated pertussis cases occurred before the scheduled date, at five months of age, for the second dose. However, nearly 39% respectively 27% of the one-dose

vaccinated cases prior to the positive sample occurred in the age interval 5 - < 12 months (where a dose 2 should have been given).

As seen in Table 31 most of the one-dose vaccinated case occurring in the age interval 5 - <12 months occurred at 5 months of age. Also remember that we use the date for the positive sample for calculation of age – generally that date is one to two weeks after onset of cough at the pertussis episode.

Table 31 Number of reported laboratory confirmed cases of pertussis from October 1, 1997 until December 31, 2007 per birth-cohort from January 1, 1996 until December 31, 2007, for unvaccinated and for children vaccinated with one dose prior to the date for the positive sample per age-group and per area for the pertussis episode.

Date of positive sample occurred in age-interval	Sweden except Göteborg				Göteborg study area			
	Not vaccinated		Vaccinated with one dose		Not vaccinated		Vaccinated with one dose	
	No.	%	No.	%	No.	%	No.	%
During 0-<1 months	55	7,1	0		23	11,7	0	
During 1-<2 months	188	24,3	0		60	30,6	0	
During 2-<3 months	205	26,5	0		59	30,1	0	
During 3-<4 months	115	14,8	79	26,6	16	8,2	22	16,7
During 4-<5 months	23	3,0	131	44,1	6	3,1	51	38,6
During 5-<6 months	11	1,4	52	17,5	0		30	22,7
During 6-<12 months	28	3,6	29	9,8	3	1,5	21	15,9
After 1 year of age	150	19,4	6	2,0	29	14,8	8	6,1
Total	775		297		196		132	

3.7 Age-specific incidence, relative risk for children with at least two doses

In Table 32 total person-time of follow-up, number of observed culture- or PCR-confirmed cases, incidence per 100 000 person years of follow-up and relative risk are calculated for different age-groups for children born from January 1, 1996 until December 31, 2007 for pertussis episodes which occurred from October 1, 1997 until December 31, 2007 in two areas of Sweden – Sweden except Gbg, and the Göteborg study area, for children who had received at least two doses of a pertussis vaccine prior to the date for the positive sample.

In Tables 33 and 34 the corresponding comparisons are performed for two birth periods; children born 1996–1998, and children born 2000 or later. For children from the Göteborg study area the first birth period means children in a nearly pure DiTeKik® cohort, while in the second birth period most children in this area have received Pentavac®, (except for children in Kungsbacka, approximately 5%, who received either Infanrix®-Polio-Hib or Pentavac®). Children born 1999 are not included in these two tables because they represent a transition cohort with mixed vaccinations within the 3-5-12 month schedule.

Table 32 Children born from **January 1, 1996 until December 31, 2007**, and followed from **October 1, 1997 until December 31, 2007** with observed Culture- or PRC-confirmed *B.pertussis* and **vaccinated with two or more doses of a pertussis vaccine** prior to the date for onset of the episode. We present Person-years of follow-up, Number of laboratory confirmed cases, Incidence per 100 000 person-years of follow-up and Relative risk of having a laboratory-verified episode of *B.pertussis* (for children in Sweden except Gbg (except the Göteborg study area) compared to children in the Göteborg study area) in the following age-/vaccine-groups at the pertussis episode; between Dose 2 and 3; and after12 months of age (after Dose 3) in ten age intervals. Age is calculated at the date of the positive culture or PCR sample.

Date of positive sample occurred	Person-years of follow-up	Number of laboratory confirmed cases	Incidence per 100 000 person-years and 95% confidence interval	Relative risk Göteborg compared to Sweden except Gbg
Between Dose 2 and 3				
Sweden except Gbg	516 635	152	29 (25-34)	-
Göteborg study area	*55 330*	*195*	*352 (304-403)*	***12.0 (9.7 – 14.8)***
After Dose 3 and				
During 1 year of age	-	-	-	-
Sweden except Gbg	875 275	72	8 (6-10)	-
Göteborg study area	*93 050*	*165*	*177 (151-205)*	***21.6 (16.3 – 28.4)***
During 2 years of age	-	-	-	-
Sweden except Gbg	806 285	114	14 (12-17)	-
Göteborg study area	*85 205*	*114*	*134 (110-160)*	***9.5 (7.3 – 15.9)***
During 3 years of age	-	-	-	-
Sweden except Gbg	715 130	105	15 (12-18)	-
Göteborg study area	*75 215*	*84*	*112 (89-138)*	***7.6 (5.7 – 10.1)***
During 4 years of age	-	-	-	-
Sweden except Gbg	624 815	105	17 (14-20)	-
Göteborg study area	*65 490*	*74*	*113 (89-142)*	***6.7 (5.0 – 9.1)***
During 5 years of age	-	-	-	-
Sweden except Gbg	536 690	96	18 (14-22)	-
Göteborg study area	*56 125*	*74*	*132 (104-166)*	***7.4 (5.4 – 10.0)***
During 6 years of age	-	-	-	-
Sweden except Gbg	452 115	122	27 (22-32)	-
Göteborg study area	*47 050*	*68*	*145 (112-183)*	***5.4 (4.0 – 7.2)***
During 7 years of age	-	-	-	-
Sweden except Gbg	369 930	108	29 (24-35)	-
Göteborg study area	*38 285*	*61*	*159 (122-205)*	***5.5 (4.0 – 7.5)***
During 8 years of age	-	-	-	-
Sweden except Gbg	289 120	90	31 (25-38)	-
Göteborg study area	*29 790*	*29*	*97 (65-140)*	***3.1 (2.1 – 4.8)***
During 9 years of age	-	-	-	**-**
Sweden except Gbg	208 930	63	30 (23-39)	**-**
Göteborg study area	*21 380*	*2*	*9 (1-34)*	***0.3 (0.1 – 1.3)***
During 10 or 11 years of age	-	-	-	**-**
Sweden except Gbg	170 885	16	9 (5-15)	**-**
Göteborg study area	*17 330*	*6*	*35 (13-76)*	***3.7 (1.4 – 9.5)***
After Dose 3 and during 1 year of age or later	-	-	-	**-**
Sweden except Gbg	5 049 175	891	18 (16-19)	**-**
Göteborg study area	*528 920*	*677*	*128 (119-138)*	***7.3 (6.6 – 8.0)***

Table 33 Children born from **January 1, 1996 until December 31, 1998**, and followed from **October 1, 1997 until December 31, 2007** with observed Culture- or PRC-confirmed *B.pertussis* and **vaccinated with two or more doses of a pertussis vaccine** prior to the date for onset of the episode. We present Person-years of follow-up, Number of laboratory confirmed cases, Incidence per 100 000 person-years of follow-up and Relative risk of having a laboratory-verified episode of *B.pertussis* (for children in Sweden except Gbg (except the Göteborg study area) compared to children in the Göteborg study area) in the following age-/vaccine-groups at the pertussis episode; between Dose 2 and 3; and after12 months of age (after Dose 3) in ten age intervals. Age is calculated at the date of the positive culture or PCR sample.

Date of positive sample occurred	Person-years of follow-up	Number of laboratory confirmed cases	Incidence per 100 000 person years and 95% confidence interval	Relative risk Göteborg study area compared to Sweden except Gbg
Between Dose 2 and 3				
Sweden except Gbg	93 035	47	51 (37-67)	-
Göteborg study area	*9 640*	*25*	*259 (168-383)*	***5.1 (3.2 – 8.3)***
After Dose 3 and				
During 1 year of age	-		-	-
Sweden except Gbg	224 875	29	13 (8-19)	-
Göteborg study area	*23 155*	*42*	*181 (131-245)*	***14.1 (8.8 – 22.6)***
During 2 years of age	-	-	-	-
Sweden except Gbg	249 215	50	20 (15-26)	-
Göteborg study area	*25 605*	*35*	*137 (95-190)*	***6.8 (4.4 – 10.5)***
During 3 years of age	-	-	-	-
Sweden except Gbg	249 215	64	26 (20-33)	-
Göteborg study area	*25 605*	*55*	*215 (162-280)*	***8.4 (5.8 – 12.0)***
During 4 years of age	-	-	-	-
Sweden except Gbg	249 215	65	26 (20-33)	-
Göteborg study area	*25 605*	*35*	*137 (95-190)*	***5.2 (3.5 – 7.9)***
During 5 years of age	-	-	-	-
Sweden except Gbg	249 215	53	21 (16-28)	-
Göteborg study area	*25 605*	*44*	*172 (125-231)*	***8.1 (5.4 – 12.1)***
During 6 years of age	-	-	-	-
Sweden except Gbg	249 215	80	32 (25-40)	-
Göteborg study area	*25 605*	*60*	*234 (179-302)*	***7.3 (5.2 – 10.2)***
During 7 years of age	-	-	-	-
Sweden except Gbg	249 215	84	34 (27-42)	-
Göteborg study area	*25 605*	*56*	*219 (165-284)*	***6.5 (4.6 – 9.1)***
During 8 years of age	-		-	-
Sweden except Gbg	249 215	83	33 (27-41)	
Göteborg study area	*25 605*	*29*	*113 (76-162)*	***3.4 (2.2 – 5.2)***
During 9 years of age	-		-	-
Sweden except Gbg	208 930	63	30 (23-39)	
Göteborg study area	*21 380*	*2*	*9 (0-26)*	***0.3 (0.1 – 1.3)***
During 10 or 11 years of age	-	-	-	-
Sweden except Gbg	170 885	16	9 (5-15)	
Göteborg study area	*17 330*	*6*	*35 (13-76)*	***3.7 (1.4 – 9.5)***
After Dose 3 and during 1 year of age or later	-	-	-	-
Sweden except Gbg	2 349 195	587	25 (23-27)	
Göteborg study area	*241 100*	*364*	*151 (136-167)*	***6.0 (5.3 – 6.9)***

Table 34 Children born from **January 1, 2000 until December 31, 2007**, and followed from **January 1, 2000 until December 31, 2007** with observed Culture- or PRC-confirmed *B.pertussis* and **vaccinated with two or more doses of a pertussis vaccine** prior to the date for onset of the episode. We present Person-years of follow-up, Number of laboratory confirmed cases, Incidence per 100 000 person-years of follow-up and Relative risk of having a laboratory-verified episode of *B.pertussis* (for children in Sweden except Gbg (except the Göteborg study area) compared to children in the Göteborg study area) in the following age-/vaccine-groups at the pertussis episode; between Dose 2 and 3; and after12 months of age (after Dose 3) in six age intervals. Age is calculated at the date of the positive culture or PCR sample.

Date of positive sample occurred	Person-years of follow-up	Number of laboratory confirmed cases	Incidence per 100 000 person years and 95% confidence interval	Relative risk Göteborg study area compared to Sweden except Gbg
	-	-	-	-
Between Dose 2 and 3	-	-	-	-
Sweden except Gbg	377 045	78	21 (16-26)	-
Göteborg study area	*40 810*	*140*	*343 (289-405)*	***16.6 (12.6 – 21.9)***
After Dose 3 and				
During 1 year of age	-	-	-	-
Sweden except Gbg	570 590	37	6 (5-9)	-
Göteborg study area	*61 540*	*90*	*146 (118-180)*	***22.6 (15.4 – 33.1)***
During 2 years of age	-	-	-	-
Sweden except Gbg	477 260	51	11 (8-14)	-
Göteborg study area	*51 235*	*55*	*107 (81-140)*	***10.1 (6.7 – 14.7)***
During 3 years of age	-	-	-	-
Sweden except Gbg	386 105	33	9 (6-12)	
Göteborg study area	*41 245*	*23*	*56 (35-84)*	***6.5 (3.8 – 11.1)***
During 4 years of age	-	-	-	-
Sweden except Gbg	295 790	34	12 (8-16)	
Göteborg study area	*31 520*	*16*	*51 (29-82)*	***4.4 (2.4 – 8.0)***
During 5 years of age	-	-	-	-
Sweden except Gbg	207 665	25	12 (8-18)	
Göteborg study area	*22 150*	*5*	*23 (7-53)*	***1.9 (0.7 – 4.9)***
During 6 or 7 years of age	-	-	-	-
Sweden except Gbg	163 990	28	17 (11-25)	
Göteborg study area	*17 395*	*1*	*6 (0-32)*	***0.3 (0.1 – 2.5)***
After Dose 3 and during 1 year of age or later	-	-	-	-
Sweden except Gbg	2 101 400	208	10 (9-11)	
Göteborg study area	*225 085*	*190*	*84 (73-97)*	***8.5 (7.0 – 10.4)***

3.7.1 Comments to incidence and risk tables

For children born from January 1, 1996 until December 31, 2007 and vaccinated with at least two doses of a pertussis vaccine prior to the date for the positive sample (Table 32), in each age-group from 5-<12 until 8 years of age, there was a statistically significant higher risk (RR=3.1 – RR=21.6) of having a laboratory confirmed episode of pertussis for children in the Göteborg study area compared to children in the rest of the country.

From 12 months of age the relative risk was 7.3 (95% C.I. 6.6 – 8.0) and the incidence figures per 100 000 years of follow-up was 128 for children in the Göteborg study area and 18 for children living outside that area. One can also note that the excess risk in Göteborg study area slowly decreases by rising age. Results in Table 32 confirm, with a larger dataset, what already was shown in Table 14 of the Part 1 analyses.

Corresponding Table 33 presents result for 389 and 634 children born January 1, 1996 until December 31, 1998 with a laboratory confirmed pertussis for children living in the Göteborg study area respectively in Sweden except Göteborg. Those children have all received at least two doses of a pertussis vaccine prior to the date of the positive sample. During this birth period children in the Göteborg area were vaccinated with the DiTeKik® vaccine and all but 24 children in the Göteborg study area in Table 33 had received that pertussis vaccine prior to the date for the positive sample.

In each age group until 8 years of age there was a statistically significant higher risk (RR=3.4 – RR=14.1) of contracting pertussis for children in the Göteborg study area compared to children in the rest of the country.

From 12 months of age the relative risk was 6.0 (95% C.I. 5.3 – 6.9) and the incidence figures per 100 000 years of follow-up was 151 for children in the Göteborg study area and 25 for children living outside that area. One can also note that the excess risk in Göteborg study area slowly decreases by age. The corresponding intent-to-treat table, Table 26, gives the same picture.

Table 34 presents result for 330 and 286 children born January 1, 2000 until December 31, 2007 with laboratory confirmed pertussis for children living in the Göteborg study area respectively in Sweden except Göteborg. Those children have all received at least two doses of a pertussis vaccine prior to the date of the positive sample. During this birth period most children in the Göteborg area were vaccinated with the Pentavac® vaccine and all but 9 children in the Göteborg study area in Table 34 had received that pertussis vaccine prior to the date for the positive sample.

In each age group until 4 years of age there was a statistically significant higher risk (RR=4.4 – RR=22.6) of receiving pertussis for children in the Göteborg study area compared to children in the rest of the country.

From 12 months of age the relative risk was 8.5 (95% C.I. 7.0 – 10.4) and the incidence figures per 100 000 years of follow-up was 84 for children in the Göteborg study area and 10 for children living outside that area. One can also note that the excess risk in Göteborg study area slowly decreases by age. The corresponding intent-to-treat table, Table 27, gives the same picture but with lower relative risks.

4. Overall rates of laboratory reported pertussis in Västra Götaland region

The yearly progress reports from the enhanced pertussis surveillance project include a section with overall information from the Swedish communicable disease reporting system. Ideally, the present Göteborg report would provide a similar overview for the Göteborg study area. However, the Swedish reporting system is county-based and therefore we can only present overall rates from the whole county of Västra Götaland (VG) but not for the Göteborg study area part of this region, representing about half of the VG population. Furthermore, the Göteborg study area includes one municipality within Halland county, representing about one quarter of the population in Halland. In other words, the national communicable disease reporting system does not allow comparisons of the Göteborg study area with the rest of Sweden.

Nevertheless, and in spite of that VG region is not a reasonable proxy for the nine VG municipalities of the Göteborg study area, we find that it valuable to look at the overall number of 3,211 laboratory reported cases from VG during the 1997-2007 period, as compared to the 13,001 laboratory reported cases from the rest of Sweden during the same time interval. We have also made some efforts to check indicators of different awareness and reporting practices in VG and in the rest of Sweden.

In addition, some performance indicators for the vaccination program were obtained within the enhanced surveillance and for these we can compare the Göteborg study area with the rest of Sweden.

Laboratory denominator data are not included in the present Swedish national reporting system. By courtesy of the county medical officers in VG and other regions, we have obtained some denominator data that were presented in the nine-year report [5], including some comparisons between laboratories within VG as well as a large city comparison of the Göteborg, Stockholm and Malmö-Lund.

4.1 Changes over time in overall number of laboratory reported cases

Figure 6 demonstrate the overall difference in number of reported cases during 1997-2007. VG region started at a lower level of reporting, having achieved a reduction in number of laboratory reported cases already in 1996 (Figure 2). Then there was a peak within the region corresponding in time to the 1999-2000 peak in all of Sweden. From 2001 through 2004, the number of reports from VG region was more or less equal to, sometimes even higher than, the number from the rest of Sweden, in spite of that the population in VG region represents 16,9% – less than 1/5 – of the Swedish population. Figure 6 also indicate that there were peaks in VG region earlier than those in Sweden in general during the two remaining of the three nationwide peaks, i.e. in 2002 and in 2004-2005. For details about laboratory reported pertussis in different age groups, see Table 37 A, giving the age-specific incidences during the years 1986-95 and 1996-2007, with the corresponding numbers in each age-group in Table 37B.

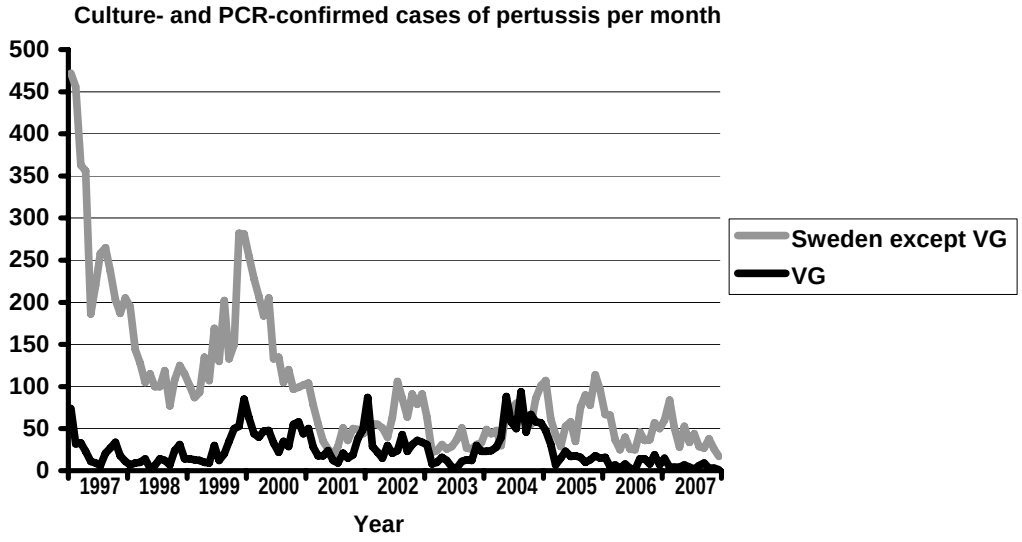

Figure 6 Number of laboratory reported cases of pertussis per month area from January 1997 through December 2007 in Västra Götaland region (black line) and the rest of Sweden (grey line).

4.2 Comparison of age-specific incidence in VG and the rest of Sweden

4.2.1 Age-specific incidences in the region of Västra Götaland and the rest of Sweden

The mean age-specific incidence of laboratory reported pertussis during the 11 period 1997-2007, i.e. after the introduction of acellular vaccines, decreased as dramatically in VG region as in the whole country (Figure 7 of the main ten year report [1]), i.e. mainly in toddlers and pre-school children. There were, however, differences in the youngest age-groups, i.e. in infants as well as in toddlers, in VG region as compared to the rest of Sweden, Figure 7.

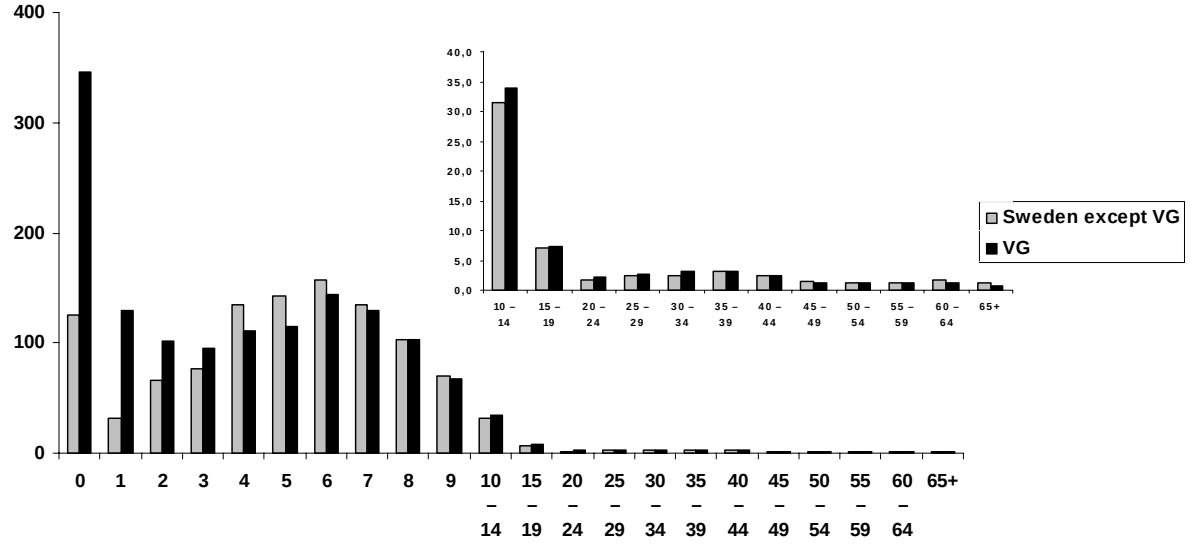

Figure 7 Mean incidence in defined age groups during 11 calendar years (1997-2006) in VG region and in the rest of Sweden after introduction of DTPa in 1996. Enlarged curves for the age groups 10 years and above are shown in the insertion.

The difference between VG region and the rest of Sweden is especially marked in infants (children below 12 months of age). Figure 8 provides the age-specific incidence in infants per calendar year in VG region and the rest of Sweden during the 1997-2007 period.

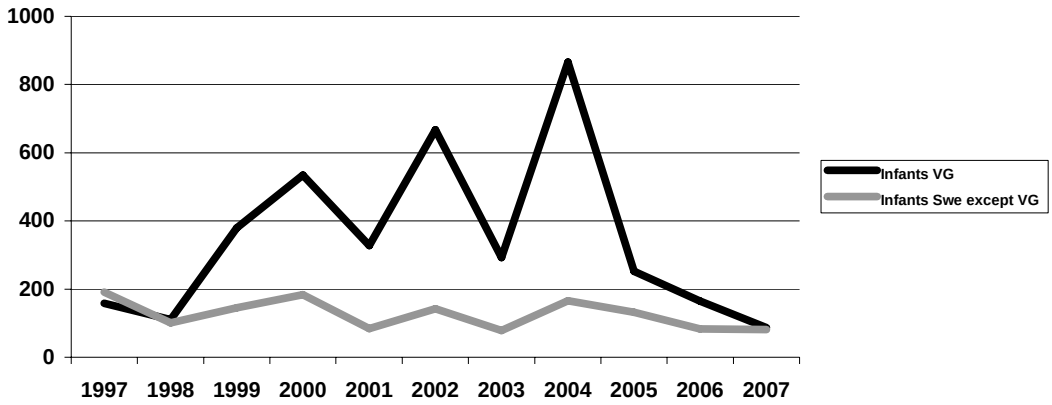

Figure 8 Age-specific incidence in infants in VG region during 10 calendar years (1986-95) before and 11 calendar years after (1997-2006) introduction of DTPa in 1996.

The incidence rates in the VG region during the outbreak years 1999-2005 were between 250 and 870/100,000 infant person years, i.e. at levels seen in Sweden before introduction of DTPa in 1996, whereas the corresponding rates in the rest of Sweden during the same time period were between 85 and 183/100,000, Table 37A. In 2007, the age-specific incidence in infancy for the first time was below 100/100,000 in VG region, but in the rest of Sweden this was achieved first time already in the calendar year of 2001. Figure 9 illustrate the infant age in month at laboratory-reported pertussis before and after

1996, and also the differences in reported number from VG region and the rest of Sweden during the years 1997-2007.

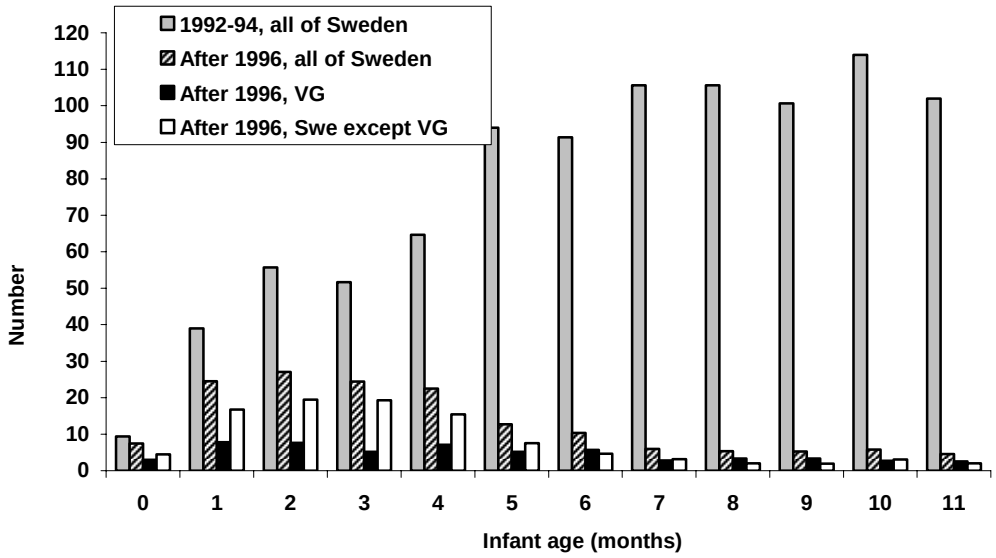

Figure 9 The mean number of infants reported in different age-groups during infant year before (grey bars) and after (striped bars) introduction of DTPa in 1996, and also the mean number of infants in the age-groups 0-11 months reported from VG region (black barns) and from the rest of Sweden (white barns) during the years 1997-2007.

Carefully note that the comparison of VG and the rest of Sweden in figure 9 is not corrected for population size.

4.3 Vaccination coverage and timing of doses

More than 99% of Swedish children attend Child Health Care. The vaccination coverage for the three first doses of Pa is in Sweden measured yearly by checking all child health care medical records. The coverage is consistently around 98.5% over the years and there are no regional differences.

The consistency over time is illustrated in Table 35, comparing the median ages (in days) at dose 1-3, and in children followed within the enhanced surveillance with the corresponding ages during the nation-wide Trial II in early 1990:s.

Table 35 Median age at dose 1-3 in Trial II (1993-94) and during the 1997-2007 enhanced surveillance period in Göteborg study area and the rest of Sweden. The scheduled ages are 3-5-12 months, corresponding to 90, 150 and 365 days.

Median ages at vaccination (days)	Dose 1 (90 days)	Dose2 (150 days)	Dose 3 (365 days)
Trial 2 (n = 72,698 infants included in 3-5-12 mo schedule)	100	174	386
Surveillance project from 1997-2007 (Sweden except Göteborg)	94	167	375
Surveillance project from 1997-2007 (Göteborg study area)	94	180	372

There was hence no difference in mean age at dose 1-3 in Göteborg and the rest of the country during the years 1997-2007. Furthermore there was no difference in mean age during these ten years and the period of Trial 2, which was a study conducted throughout Sweden during "ordinary circumstances", i.e. at the infants ordinary child health care centre. The consistency in timing of the three infant doses is further illustrated in Figure 9, by plotting the cumulative proportion of children who have received their first, second and third dose in relation to scheduled age 3-5-12 months.

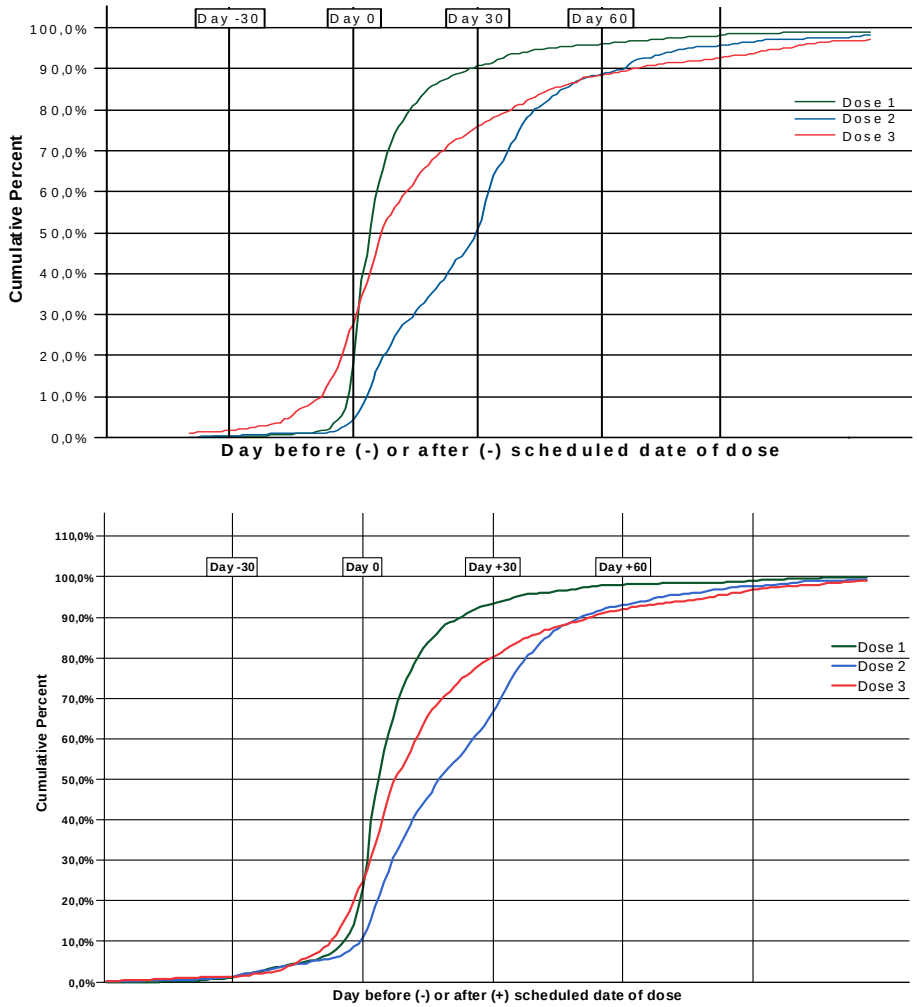

Figure 10 Cumulative proportion of children in the Göteborg study area (upper figure) in the rest of Sweden (lower figure) vaccinated in relation to scheduled day (Day 0) for the doses at 90 days, 150 days and 365 days. Data from the enhanced ten year surveillance. Vaccination status of children born from January 1, 1996 and until December 31, 2007 with a culture- or PCR-reported episode of pertussis between October 1, 1997 and December 31, 2007.

The "deviations" from scheduled ages were about the same in the Göteborg study area and in the rest of Sweden. However, Dose 2 seems to be administered somewhat later for children in the Göteborg study area compared to the rest of Sweden.

4.4 Catch-up vaccinations

Infants born during the latter part of 1995 were vaccinated against pertussis in most parts of the country, because the start of their vaccination program was delayed until the Pa vaccines were licensed in January 1996. At age 2 years, the overall 3-dose coverage for the 1995 cohort was 60%. Toddlers and school children were catch-up vaccinated to some degree in Sweden except Göteborg study area, but a true catch-up was only implemented in this area of the VG region. In this city area, free catch-up vaccinations to more than 65,000 children born in the 1990:s were offered from 1997 to 1999. By spring 2000, about 56% of children born in the 1990:s were vaccinated with three doses of Pa-containing vaccine [4]

The influence of the Göteborg catch-up vaccinations on the long-term circulation of *Bordetella pertussis* is not known. The mass vaccination study reported signs of herd immunity as reflected by a significant reduction of the number of pertussis cases in vaccinated and unvaccinated individuals during the 1997-1999 period, but the follow-up stopped at the same time as the mass vaccination campaign stopped [4].

4.5 Reporting routines

Pertussis cases are reported either by clinicians or by microbiological laboratories, or both ways, according to the Communicable Disease Act. The proportion of laboratory reports (i.e. cases reported both from clinicians and from laboratories, or only from the laboratories) is somewhat higher in the VG region than in the rest of Sweden, Figure 11.

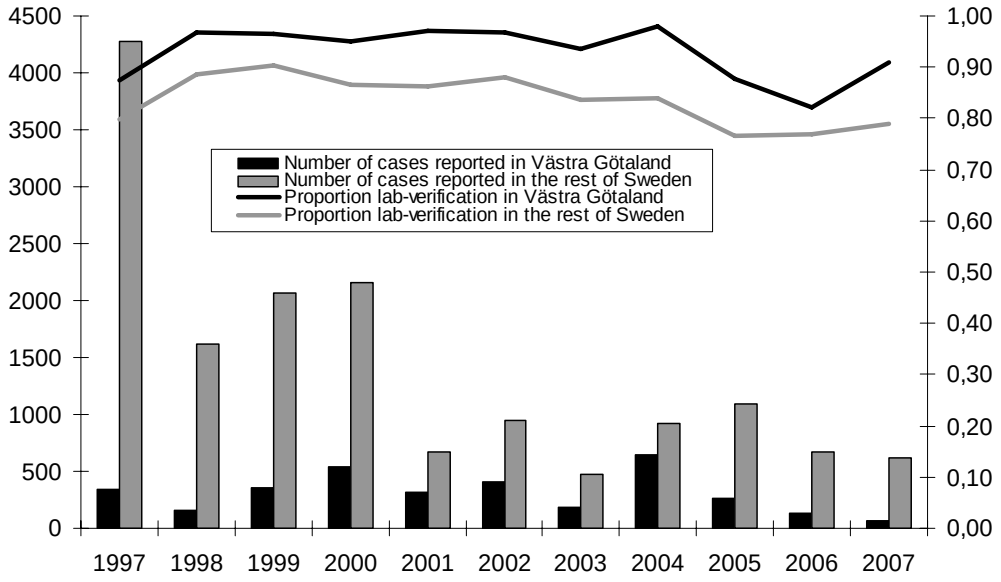

Figure 11 The proportion laboratory reported pertussis in relation to the overall number of cases reported 1997-2006 in Göteborg study area and the rest of Sweden.

4.6 Case ascertainment

Confirmation of *B. pertussis* by culture is in Sweden slowly by slowly becoming replaced by PCR, although many laboratories have continued to perform cultures on PCR-positive samples. In 1997 the proportion of PCR-verified cases was 5% or less. In 2003 around 20% of all laboratory reports were based on PCR and nowadays only about 50% of the pertussis reports are based on culture. It is well known that PCR may have a higher sensitivity in comparison with culture, especially in milder cases and later stage of disease, and the increasing use of PCR may hence increase the reporting of cases. By courtesy of the dept of communicable disease in Västra Götaland, we obtained nominator and denominator results form the four major laboratories in the region during the period 1997-2006, and also from one smaller private laboratory. These data are presented in the nine year Göteborg report [5].

4.7 Potential differences in awareness

One possibility to address awareness would be to analyse laboratory denominator data, i.e. the number of samples submitted for detection of *B. pertussis* by culture or PCR in different parts of the country. By courtesy of the dept of Communicable Disease Control in Stockholm, we obtained the total number of samples submitted during the year of 2006 to three major Stockholm laboratories (Capio, Huddinge, Karolinska including Medilab) for detection of *B. pertussis* by culture or PCR, see nine year Göteborg report, Table 36 [5]. The table also gives the sum of samples analysed within VG region and at the Göteborg laboratory during this year.

There are no studies addressing the awareness of pertussis among the reporting physicians, but there are examples of high reporting rates with a timely association to media attention or to medical information campaigns drawing attention to pertussis. In the region of VG there was an increased reporting after an illustration of an infant case on the cover of the local newspaper during early summer 2004, see nine year Göteborg report, Figure 14 [5].

Table 37A Overall and age-specific incidence[5] of laboratory-reported pertussis per 100,000 in the region of Västra Götaland, from 1986 to 1995 before introduction, and 1996 to 2007 after introduction of acellular pertussis vaccine in Sweden. Data on number of reported cases were lost during two months of the year 1990 and therefore the denominator used for incidence was 10/12 of the 1990 population

	1986	1987	1988	1989	1990*	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007
All ages	**162,0**	**178,6**	**183,7**	**108,6**	**101,8**	**124,9**	**102,1**	**141,5**	**160,9**	**150,5**	**62,7**	**20,1**	**10,2**	**23,1**	**34,7**	**20,1**	**26,3**	**11,4**	**41,7**	**15,1**	**6,8**	**4,0**
0	1345,0	1296,6	1301,6	750,3	754,5	925,2	581,8	885,7	1052,1	992,9	**427,9**	**158,1**	**110,1**	**379,2**	**534,1**	**327,9**	**667,7**	**292,4**	**865,6**	**251,8**	**164,9**	**87,5**
1	2178,0	2142,3	2342,3	1279,3	1076,9	1293,1	1047,8	1622,6	1715,9	1617,2	590,6	**118,8**	**50,4**	**115,9**	**383,1**	**129,2**	**217,2**	**62,7**	**248,5**	**82,5**	**29,1**	**11,3**
2	2208,9	2417,2	2492,0	1435,0	1273,1	1649,7	1302,0	1512,5	1943,6	1810,9	602,8	201,2	**35,7**	**50,4**	**141,4**	**168,0**	**192,8**	**57,3**	**206,4**	**36,3**	**23,5**	**11,6**
3	2176,9	2556,9	2468,5	1430,8	1344,7	1713,8	1201,0	1556,5	1952,1	1602,7	649,2	202,8	92,4	**83,2**	**157,0**	**121,5**	**135,0**	**25,6**	**114,2**	**62,4**	**30,1**	**5,9**
4	1742,4	1994,4	1930,9	1370,3	1196,5	1208,7	1053,6	1486,4	1549,4	1647,9	681,7	261,9	106,7	141,2	**148,0**	**106,5**	**121,0**	**51,2**	**191,2**	**19,0**	**12,5**	**18,0**
5	1431,7	1540,0	1614,6	980,3	733,2	869,7	798,2	1246,6	1080,3	1036,4	511,6	174,1	77,7	121,9	249,2	**70,7**	**149,6**	**38,1**	**280,7**	**31,8**	**25,3**	**18,6**
6	1117,9	1227,0	1079,2	613,0	636,9	744,1	613,5	687,9	622,3	797,7	463,4	130,5	89,6	276,8	217,8	178,1	**146,5**	**55,9**	**322,9**	**101,7**	**6,3**	**25,1**
7	398,4	740,9	568,5	310,3	261,3	264,3	318,0	434,0	498,2	523,2	268,9	109,8	74,5	192,8	241,8	151,4	150,4	**70,0**	**260,2**	**75,9**	**31,7**	**31,5**
8	269,1	288,0	399,8	155,3	177,7	247,6	116,3	187,5	282,2	246,6	94,0	69,6	38,1	148,8	201,7	134,8	105,5	59,0	**233,2**	**74,3**	**31,5**	**0,0**
9	175,1	147,2	159,5	118,0	103,7	79,8	86,3	127,8	139,0	168,0	93,1	15,6	34,7	52,4	139,0	84,1	95,9	60,1	160,2	**52,3**	**12,3**	**6,3**
10	161,7	74,9	101,9	19,0	51,8	73,8	36,7	79,6	24,1	103,4	61,5	16,4	10,4	79,3	109,0	32,3	55,8	14,3	114,8	79,9	**46,3**	**12,2**
11	67,8	65,8	87,1	31,7	7,6	49,2	12,2	30,4	121,2	41,8	5,7	5,6	5,5	52,0	74,1	51,9	32,2	37,1	81,1	39,9	5,3	**11,5**
12	65,8	11,3	11,9	37,1	15,1	25,1	18,4	42,7	18,1	30,0	11,9	11,4	11,1	32,7	41,4	44,2	37,6	27,5	88,0	76,2	24,8	5,3
13	10,8	49,2	28,1	17,8	7,4	18,8	6,3	18,3	30,2	0,0	0,0	0,0	5,7	22,2	48,8	10,3	29,4	32,8	68,5	46,1	14,2	14,9
14	10,7	10,8	0,0	11,2	7,1	24,6	6,3	12,5	30,2	0,0	6,0	0,0	0,0	17,1	16,6	10,8	20,5	4,9	42,0	22,8	4,6	9,4
15	16,3	21,4	32,3	10,9	13,4	0,0	6,1	6,2	18,5	0,0	0,0	0,0	6,0	17,7	5,7	11,0	10,7	5,1	14,6	18,6	13,6	13,8
16	16,4	5,4	21,4	0,0	19,4	5,5	0,0	6,1	18,5	12,3	6,0	5,9	5,9	5,9	41,2	5,6	10,9	5,3	20,3	29,1	4,6	0,0
17	10,6	32,7	21,6	0,0	6,4	0,0	5,5	17,5	0,0	6,1	6,1	6,0	0,0	0,0	0,0	0,0	0,0	0,0	10,6	5,1	4,8	13,8
18	0,0	5,3	16,2	0,0	0,0	5,3	5,3	0,0	5,8	0,0	0,0	0,0	0,0	0,0	11,7	0,0	5,8	0,0	16,2	0,0	10,1	4,8
19	4,8	9,9	5,2	5,3	0,0	5,2	0,0	5,3	5,4	0,0	5,9	0,0	0,0	5,9	11,7	0,0	0,0	5,8	5,5	10,8	5,3	5,0
20-24	17,5	10,3	13,9	5,6	1,1	4,9	5,0	6,1	13,2	4,1	2,1	1,1	1,1	3,4	1,1	1,1	2,3	0,0	8,8	2,2	0,0	2,1
25-29	29,0	31,0	26,5	12,8	20,5	13,8	14,3	13,3	15,3	11,9	4,7	2,9	1,0	2,9	1,9	2,0	2,0	2,0	8,2	3,1	3,1	0,0
30-34	20,5	20,4	28,5	16,2	14,6	17,2	22,3	16,1	27,3	13,2	8,2	0,0	0,9	0,9	4,6	2,8	4,7	1,0	12,4	5,7	1,9	0,0
35-39	9,4	12,6	17,8	9,1	8,6	8,2	1,0	9,1	14,1	15,1	8,1	0,0	3,0	0,0	7,6	1,8	4,5	3,5	7,1	7,3	0,0	0,0
40-44	4,9	5,6	8,3	4,6	5,5	3,8	7,7	4,9	9,1	3,1	0,0	0,0	0,0	0,0	1,0	2,0	4,0	2,0	10,7	3,8	2,7	0,0
45-49	3,8	3,7	4,7	3,3	6,3	1,0	0,9	3,7	7,4	1,9	2,8	1,0	1,0	0,0	0,0	0,0	2,0	2,0	4,0	2,0	1,0	1,0
50-54	9,9	8,5	15,3	2,7	7,9	7,7	7,5	7,1	3,4	3,2	2,0	1,9	0,0	0,9	0,0	1,0	2,0	0,0	2,0	3,1	2,1	1,0
55-59	4,1	8,3	2,8	1,4	8,6	1,4	5,8	12,8	9,7	2,7	2,6	0,0	0,0	0,0	2,2	0,0	1,0	1,9	3,8	1,0	2,9	0,0
60-64	3,8	13,2	5,4	1,4	5,1	12,8	11,5	5,8	3,0	6,0	1,5	1,5	0,0	0,0	1,4	0,0	0,0	1,3	2,4	4,5	1,1	1,0
65+	3,6	3,6	4,3	1,6	0,9	3,1	4,6	3,5	4,6	3,8	1,9	0,8	0,4	0,8	1,2	0,8	0,8	0,8	0,8	0,4	0,8	0,8

[5] Note! Age specific incidence figures in black bold (upper right corner of table) concern children born 1996 or later, i.e. children born after introduction of Pa vaccine in Sweden: Note that the age specific incidence figures concern individuals from two yearly birth cohorts Figures in red represent children born 1995 (latter part) or 1996 (early part), i.e. those born at time of introduction of Pa vaccines. Most of these were vaccinated. All other incidence figures concern birth cohorts born before introduction of Pa vaccine in Sweden. For vaccine coverage per birth cohort, see main report [1] figure 10.

Table 37B Number of laboratory reported cases[6] of pertussis from the region of Västra Götaland in defined age-groups from 1986 to 1995 before introduction and 1996 to 2007 after introduction of acellular pertussis vaccine in Sweden. Data on reported cases for the year 1990 represents only ten months, because data from two of the 1990 months were accidently lost during a process of data transferral between two national computer databases.

	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007
All ages	**2269**	**2514**	**2600**	**1548**	**1219**	**1804**	**1482**	**2066**	**2367**	**2227**	**930**	**299**	**151**	**343**	**518**	**301**	**395**	**173**	**633**	**231**	**105**	**62**
0	229	228	242	147	130	197	123	183	208	183	72	**25**	**17**	**58**	**82**	**51**	**106**	**48**	**146**	**43**	**29**	**16**
1	361	368	414	238	176	267	223	343	354	320	109	20	**8**	**18**	**59**	**20**	**34**	**10**	**41**	**14**	**5**	**2**
2	351	402	429	254	198	324	268	321	411	374	119	37	6	**8**	**22**	**26**	**30**	**9**	**33**	**6**	**4**	**2**
3	343	408	412	247	199	320	236	321	417	341	134	40	17	14	**25**	**19**	**21**	**4**	**18**	**10**	**5**	**1**
4	277	316	310	230	173	215	197	293	322	354	145	54	21	26	25	**17**	**19**	**8**	**30**	**3**	**2**	**3**
5	228	246	257	158	103	151	142	234	215	217	110	37	16	24	46	12	**24**	**6**	**44**	**5**	**4**	**3**
6	178	196	173	98	86	126	107	123	118	160	97	28	19	57	43	33	25	**9**	**51**	**16**	**1**	**4**
7	62	118	91	50	35	43	54	76	90	100	54	23	16	41	50	30	28	12	**42**	**12**	**5**	**5**
8	42	45	64	25	24	40	19	32	50	45	18	14	8	32	43	28	21	11	40	**12**	**5**	**0**
9	28	23	25	19	14	13	14	21	24	30	17	3	7	11	30	18	20	12	30	9	**2**	**1**
10	27	12	16	3	7	12	6	13	4	18	11	3	2	16	23	7	12	3	23	15	8	**2**
11	12	11	14	5	1	8	2	5	20	7	1	1	1	10	15	11	7	8	17	8	1	2
12	12	2	2	6	2	4	3	7	3	5	2	2	2	6	8	9	8	6	19	16	5	1
13	2	9	5	3	1	3	1	3	5	0	0	0	1	4	9	2	6	7	15	10	3	3
14	2	2		2	1	4	1	2	5	0	1	0	0	3	3	2	4	1	9	5	1	2
15	3	4	6	2	2	0	1	1	3	0	0	0	1	3	1	2	2	1	3	4	3	3
16	3	1	4	0	3	1	0	1	3	2	1	1	1	1	7	1	2	1	4	6	1	0
17	2	6	4	0	1	0	1	3	0	1	1	1	0	0	0	0	0	0	2	1	1	3
18	0	1	3	0	0	1	1	0	1	0	0	0	0	0	2	0	1	0	3	0	2	1
19	1	2	1	1	0	1	0	1	1	0	1	0	0	1	2	0	0	1	1	2	1	1
20-24	18	11	15	6	1	5	5	6	13	4	2	1	1	3	1	1	2	0	8	2	0	2
25-29	28	30	26	13	18	15	16	15	17	13	5	3	1	3	2	2	2	2	8	3	3	0
30-34	20	20	28	16	12	17	22	16	28	14	9	0	1	1	5	3	5	1	13	6	2	0
35-39	10	13	18	9	7	8	1	9	14	15	8	0	3	0	8	2	5	4	8	8	0	0
40-44	5	6	9	5	5	4	8	5	9	3	0	0	0	0	1	2	4	2	11	4	3	0
45-49	3	3	4	3	5	1	1	4	8	2	3	1	1	0	0	0	2	2	4	2	1	1
50-54	7	6	11	2	5	6	6	6	3	3	2	2	0	1	0	1	2	0	2	3	2	1
55-59	3	6	2	1	5	1	4	9	7	2	2	0	0	0	2	0	1	2	4	1	3	0
60-64	3	10	4	1	3	9	8	4	2	4	1	1	0	0	1	0	0	1	2	4	1	1
65+	9	9	11	4	2	8	12	9	12	10	5	2	1	2	3	2	2	2	2	1	2	2

[6] Note! Age specific numbers in black bold (upper right corner of table) concern children born 1996 or later, i.e. children born after introduction of Pa vaccine in Sweden: Note that the age specific numbers concern individuals from two yearly birth cohorts. Figures in red represent children born 1995 (latter part) or 1996 (early part), i.e. those born at time of introduction of Pa vaccines. Most of these were vaccinated. All other numbers concern birth cohorts born before introduction of Pa vaccine in Sweden. For vaccine coverage per birth cohort, see main report [1] figure 10.

5 Plan for continued work

Study objectives from 2008:
- To study the long-term effects of a general infant acellular pertussis vaccination program implemented in 1996, with addition of a pre-school booster from 2007, on age-specific incidence in vaccinated cohorts and in the general population.
- To find background data for suitable interval until next booster

In addition, analyses will from 2008 focus on
- pertussis in infants and boosted age cohorts, in order to monitor the impact of preschool booster on age-specific incidence in infants and
- the duration of protection from pre-school booster.

Additional studies may be added to the project as decided by the yearly steering committee meetings:
- Mathematical modelling, capture-recapture analyses or other additional analyses

Yearly progress reports will as previously summarize overall number and age-specific incidence of laboratory confirmed cases, detailed analyses in vaccinated cohorts, including hospital admission rates, and number of cases in trial cohorts, and procurement of vaccine per county will be provided. In addition, case-contact information will be added for infants. Progress reports will be based on data collected per calendar year

Scientific publications and presentations:
- Manuscripts planned during project year 11 include an overall 10 year project summary, with 10 year data concerning Göteborg presented separately, and a presentation of clinical information, including data from cohorts no longer under surveillance (overall clinical presentation of pertussis), and analyses of antibiotic use in relation to severity of disease and duration of symptoms
- An international workshop on pertussis epidemiology will be organised in Stockholm November 19-21, 2008

6 Administration

Contracts for the project Pertussis surveillance in Sweden have been agreed for continued follow-up of clinical epidemiology during year 2004 to 2006 with the participating manufacturers, Sanofi-Pasteur-MSD, Lyon, Sanofi-Pasteur, Canada, and Glaxo SmithKline, Belgium.

The Advisory Group met annually. Progress reports are prepared as post marketing follow-up for regulatory agencies. For transparency, it has been agreed that annual progress report is posted on www.smittskyddsinstitutet.se. The two vaccine specific Appendices 2 should also be posted, with a clear note of caution that comparisons between vaccines should not be performed.

The advisory group should in advance approve public presentations of data from the study. Papers should be submitted to peer reviewed journals. The investigators and the Advisory Group will not endorse other uses of the data.

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Aktuella rapporter i denna serie

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