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Low varicella-related consultation rate in the Netherlands in primary care data ☆

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ABSTRACT

Background

In the Netherlands, a relatively low varicella disease burden compared to other European countries is observed within routine surveillance. To validate this, we estimated the varicella-related consultation rate using The Integrated Primary Care Information database.

Methods

In this retrospective cohort study, varicella patients in 2006–2008 were identified by the International Classification of Primary Care (A72) and free text in the electronic medical records, and manually reviewed to be categorised as ‘varicella’ or ‘probable varicella’. The incidence of GP-consultation, specialist referral, emergency department contact and hospitalisation due to varicella was calculated, standardised to the Dutch population.

Results

We identified 1881 varicella cases (2348 including probable cases), 14 patients were hospitalised. The overall incidence of GP-consultation due to varicella per 100,000 person-years was at least 281 (95%CI 268–294) and when probable cases were also included at maximum 354 (95%CI 340–369). The overall incidence of specialist referral, emergency department contact and hospitalisation per 100,000 person-years was 3.9 (95%CI 2.7–5.6), 2.5 (95%CI 1.5–4.0) and 2.0 (95%CI 1.2–3.4) respectively.

Conclusions

This study confirms the relatively low disease burden due to varicella in the Netherlands. In this study, using primary care data, similar incidences of GP consultation and referral to secondary care due to varicella were found as in routine surveillance. The lower varicella-related consultation rate might be linked to more conservative GP consultation behaviour in the Netherlands, and the relatively young age of infection. This is highly relevant for the decision-making process whether or not to introduce universal childhood varicella vaccination in the Netherlands.

ABBREVIATIONS

CI, Confidence interval;
GP, General practitioner;
ICPC, International Classification of Primary Care;
IPCI, Integrated Primary Care Information;
IR, Incidence rate;
LMR, National Medical Register;
VZV, varicella zoster virus

1. INTRODUCTION

Varicella is a highly contagious disease caused by primary infection with the varicella zoster virus (VZV). Although varicella is generally considered a mild disease, it may lead to serious complications, hospitalisation and sometimes even death [1]. In 2004, the European Working Group on Varicella (EuroVar) recommended varicella vaccination to all healthy children between 12 and 18 months and to all susceptible children before their 13th birthday [2]. In view of the increased severity with age there was also consensus that routine vaccination should be implemented only if a high level of vaccine coverage can be reached over a reasonable period; if not, vaccination of susceptible adolescents was suggested as an alternative option. In Germany, Luxembourg, Latvia, Greece and Cyprus childhood varicella vaccination is already included in the National Immunisation Programme (NIP) and in some other European countries, varicella vaccination is only offered in specific regions, only in the private sector, or only to high-risk groups and/or susceptible adolescents [3], [4] and [5]. In the Netherlands, vaccination against varicella has not been implemented in the NIP yet.

In the decision-making process whether or not to introduce universal childhood varicella vaccination, insight into the severity and extent of the national disease burden of varicella is essential [6]. In the Netherlands, nearly 100% of the population contract the varicella zoster virus [7]. However, in the context of varicella vaccination and its cost-effectiveness the focus is not necessarily on prevention of varicella but on prevention of severe varicella complications. So on prevention of the more severe varicella patients who need healthcare or die. Patients who do not consult a GP probably experience milder symptoms and do not cause considerable direct healthcare costs. According to routine surveillance data (Appendix 1), the reported number of varicella related general practitioner (GP) consultations, hospital admissions and/or deaths per 100,000 inhabitants in the Netherlands are lower

compared with other countries, such as the United States, England and Wales and Germany (pre-vaccine area) [8]. However, a recent Dutch study found an incidence of GP consultations due to varicella in 2004–2008 of 515 per 100,000 [9], almost twice as high as found in the routine surveillance.
With regard to the decision whether or not to introduce universal childhood varicella vaccination in the Netherlands, it is important to have robust estimates of the incidence of varicella-related consultations in healthcare to validate the lower estimates obtained through routine surveillance. Therefore, we performed a retrospective cohort study in the dynamic population of the Integrated Primary Care Information (IPCI) database to investigate the incidence of GP-consultations, referral to specialists, contacts with emergency departments and hospitalisations due to varicella.

2. Materials and methods

2.1. Setting

The IPCI database is a longitudinal GP research database from the Erasmus University Medical Center, Rotterdam for which data collection started in 1996. The electronic database presently contains over 1 million patient records from more than 400 GPs in the Netherlands [10], [11] and [12]. The IPCI database contains comprehensive information on the medical history of patients, including referral to secondary healthcare. The medical records of patients in IPCI are anonymised and contain information on demographics, signs and symptoms, diagnoses (using the International Classification of Primary Care (ICPC) codes), clinical findings, laboratory test results, drug prescriptions, referral to specialists and hospitalisation. Summaries of letters from specialists and hospital discharge letters are also included within free text fields and a hard copy of the original letter can be provided upon request. The patient population is nationally representative by sex and age, except for a slight under representation of the elderly population moving to nursing homes. IPCI complies with European Union guidelines on the secondary use of healthcare data for medical research and has been proven valid for pharmaco-epidemiological research. Guidelines on good pharmaco-epidemiological research are rigorously followed by all researchers working on the IPCI database. The use of IPCI data for the current study was approved by the Scientific and Ethical Advisory Group of the IPCI database (project number 07/44).

2.2. Study population

The total study population for the current study comprised all persons with a patient record in the IPCI database in the period between January 2006 and December 2008. All persons had at least 1 year of valid database history, which means that the GP practice contributed data to the IPCI database for at least 1 year and the patient had been registered with the GP for at least 1 year. Follow up ended on the date the person transferred out of the practice, on the date of last data supply by the GP, the date of death, the date of varicella diagnosis (or first onset of symptoms) or 31 December 2008 at latest.

2.3. Methods

Varicella cases in IPCI were identified according to the following procedure: all patients with diagnosis ICPC-code A72 (=varicella/chickenpox) and all patients with

chickenpox (Dutch: 'waterpokken'), varicella or VZV in the free text fields in the medical journal were considered to be potential varicella cases. Subsequently, all these patients were manually reviewed by (bio)medical students and categorised as 'varicella' or 'probable varicella' cases (if the GP was not sure of the diagnosis). For all (probable) varicella cases additional medical information related to varicella was collected from the medical journal text:
- ICPC-code.
- Number and type of GP visits (consultation at GP practice, telephone consultation, GP visit at home, consultation at central GP point outside normal working hours).
- Prescription of medication.
- Complications.
- Referral to secondary healthcare (specialist, emergency department or hospital admission).

If the type of GP visit was not specified, we chose for a consultation at the GP practice, because this was the most common consult type. Possible complications of varicella were included if they occurred within 4 weeks of the date of first symptom onset (or if not available the diagnosis date). In cases of doubt, a medical doctor reviewed the possible complication indicated by the (bio)medical student to judge if it was likely to be caused by varicella.
For varicella patients (n = 54) that were referred to a specialist, emergency department or admitted in a hospital, a short questionnaire was sent to the GP in order to confirm the (date of) varicella diagnosis, the (main reason for the) referral to a specialist, emergency department or hospital admission and complications due to varicella; for 12 of these 54 patients it was not possible anymore to contact the GP. Additionally, for this subgroup of patients anonymous copies of specialist and hospital discharge letters were collected to verify if the collected information based on the electronic patient record was correct and complete.

2.4. Data analysis

Incidence rates (IR) of GP consultation, specialist referral, emergency department contact and hospitalisation due to varicella were calculated by dividing the total number of varicella cases by the total number of person-years within the study population. IRs and 95% confidence intervals (CI) were calculated by calendar year, sex and age. For the incidence of GP consultation, we calculated a *minimum* IR in which only varicella cases were included and also a *maximum* IR in which all probable cases were included as well (see also Fig. 1). Additionally, all IRs were standardised (direct standardisation) by sex and age to the mean Dutch population in the period 2006–2008 to be able to compare our results with routine surveillance data. IRs were calculated by using Jerboa© software (developed by the Erasmus University Medical Center, Rotterdam).

[FIGURE 1]

Descriptive analyses were used to present the additional medical information regarding number and type of GP visits, prescription of medication, complications and referral to secondary healthcare. Differences in characteristics between varicella cases and probable varicella cases were tested using Pearson's χ^2 or Fisher's exact test. The analyses were performed using SPSS 19.0. To correct for multiple testing, the Benjamini–Hochberg method was applied with a false discovery rate of 0.05.

3. RESULTS

3.1. Study population

The total study population of IPCI in the period 2006–2008 consisted of 630,726 subjects who contributed a total of 740,494 person-years of follow-up. Within this study population, 3725 potential varicella patients were identified by the ICPC-code and free text fields. After manual review, 1881 varicella cases and 467 probable varicella cases remained, 14 cases were hospitalised. Of the 1377 potential varicella patients that were rejected, 63% appeared to be no varicella patients, 12% had only been in contact with a (probable) varicella patient, 6% concerned herpes zoster patients and for 18% it was unclear if the diagnosis was varicella (see Fig. 1).
For only 61% of the 2348 (probable) varicella cases the ICPC-code for varicella (A72) was registered as diagnosis code in the medical record. As expected, this percentage was higher among varicella cases (67%) than among probable varicella cases (37%) (Table 1). For an additional 5% of the (probable) cases, the ICPC-code A72 was not used as the diagnosis code but was mentioned at another place in the medical record. If we would have selected varicella cases based on the ICPC-code only, we would have missed 816 (probable) varicella cases that were linked to another ICPC-code and we would have included 229 additional cases that were rejected as varicella cases after manual validation (see Table 2).

[TABLE 1]

[TABLE 2]

3.2. Incidence rates

The overall *minimum* age-sex standardised IR for GP consultation due to varicella in IPCI in the period 2006–2008 was 281 (95%CI 268–294) per 100,000 person-years, the *maximum* age-sex standardised IR was 354 (95%CI 340–369) per 100,000 person-years (Table 3). The IR for GP consultation was highest in the age groups <5 years (Fig. 2). The overall age-sex standardised IR for specialist referral, emergency department contact and hospitalisation due to varicella in IPCI in the period 2006–2008 was 3.9 (95%CI 2.7–5.6), 2.5 (95%CI 1.5–4.0) and 2.0 (95%CI 1.2–3.4) per 100,000 person-years respectively. The overall age-sex standardised IRs in IPCI were somewhat higher than the crude estimates (Table 3).

[TABLE 3]

[FIGURE 2]

3.3. Healthcare use of (probable) varicella cases

Of all (probable) varicella cases, 81% consulted the GP at the practice, 22% had a telephone consultation with the GP practice, 10% went to a central GP point for a consultation (outside normal working hours of the own GP practice) and only 0.3% were visited at home by the GP (Table 1). Among probable varicella cases the proportion with telephone contact was higher (32% versus 19%) and the proportion with a consultation at the GP practice lower (66% versus 84%) than among varicella cases.

Most patients contacted their GP just because of the typical clinical picture of varicella (fever and itching vesicles). Varicella complications were recorded in 21% of all cases (26% among 0-year-olds, 23% among 1–4-year-olds and 13% among 5+-year-olds) and occurred less frequently in probable cases (11% versus 24%). Complications most often mentioned were bacterial super infection of skin lesions (7% of all (probable) varicella cases), otitis media (5%), pharyngitis/tonsillitis (4%), conjunctivitis (2%) and gastroenteritis (1%); neurological complications were seen in 0.5% (Table 4). Bacterial super infection, pharyngitis/tonsillitis, and gastroenteritis occurred more frequently in cases than in probable cases.

[TABLE 4]

Medication related to (complications of) varicella was prescribed to 54% of all cases, more often in cases than in probable cases (56% versus 42%). Most often prescribed medication concerned local skin medication (pruritus control and general skin care; 31%), antipyretics (11%) and antimicrobials (systemic (8%) or local (7%)) (Table 5).

[TABLE 5]

The referral to secondary healthcare was 2% (4% among 0-year-olds, 2% among 1–4-year-olds and 1% among 5+-year-olds); 98% of the (probable) varicella cases were treated by the GP only, 1.1% were referred to a specialist (paediatrician $n = 15$, dermatologist $n = 5$, radiologist $n = 2$, ophthalmologist $n = 2$, ENT (ear, nose throat) specialist $n = 1$, neurologist $n = 1$ and other $n = 2$), 0.7% contacted the emergency department of a hospital and 0.6% were admitted in a hospital due to varicella (Table 1). The hospitalised varicella patients in this study were admitted because of various reasons: (imminent) dehydration ($n = 7$), very high/persisting fever ($n = 4$), febrile convulsions ($n = 3$), bacterial super infection ($n = 2$), shortness of breath ($n = 2$) and/or encephalitis ($n = 1$). The proportion of cases referred to secondary healthcare in general (2.6%) and to a specialist (1.4%) in particular was higher than the proportion of referred probable cases (0%).

4. DISCUSSION

The overall incidence of GP-consultations due to varicella per 100,000 person-years was at least 281 and when probable cases were also included at maximum 354. Complications were recorded in one fifth of all (probable) varicella cases that consulted a GP and were usually mild. Therefore, the referral to secondary healthcare was limited: most cases were treated by the GP alone. In more than half of the (probable) cases medication related to (complications of) varicella was prescribed but in most cases it concerned local skin medication and antipyretics (over the counter (OTC) drugs).

The *minimum* incidence estimates for GP consultations and hospitalisations of the current IPCI study are comparable with the routine surveillance estimates (see Appendix 1). Thus, our study showed no indication of considerable underreporting of varicella-related consultations in routine surveillance in the Netherlands. These results also confirm the relatively low varicella-related consultation rate in the Netherlands compared to other countries [8]. The differences compared with other countries could be attributed to differences in the VZV epidemiology, differences between national surveillance systems, the healthcare system or healthcare seeking

behaviour. It is known that the mean age of primary VZV infection in the Netherlands is lower than in other countries, and according to literature the risk of complications rises with age (with exception of the 0-year-olds) [13] and [14]. A previous study also showed that the Dutch hospitalisation rate is higher among older age groups, except for the 0-year-olds [15]. In the current study with only 14 hospital admissions (all <5 years of age) accurate estimation of the hospitalisation rate by age was not possible. Furthermore, the percentage of complications among GP consultations in our study was highest among 0-year-olds and lowest among individuals aged 5 years and older. So these figures do not indicate increased severity with age. It is important to keep in mind that the number of GP consultations and hospitalisations do not reflect the full disease burden due to varicella although patients who do not consult a GP experience probably milder symptoms and do not cause considerable direct healthcare costs. Fleming stated that in the Netherlands 32% of incident varicella cases did not consult a GP, which was quite high compared with Portugal (20%) and England and Wales (14%) [16]. Wolleswinkel-van den Bosch et al. found that even 62% of the Dutch parents within their internet survey did not consult a physician when their child was ill with varicella [17]. In the Netherlands, most questions around generic varicella symptoms (mainly pruritus and fever) are answered telephonically by the practice assistant or the local pharmacy and may not be recorded with an ICPC-code in the medical records. Because treatment of symptoms like pruritus and fever can often be managed at home with over the counter (OTC) drugs which are not reimbursed, consulting a physician, in order to get a prescription, is not needed. The relatively low incidence estimates for GP consultations and hospitalisations, that might be linked to the relatively young age of infection [7] and [15], and the more conservative GP consultation behaviour in the Netherlands [16], will influence a cost-effectiveness analysis regarding universal childhood varicella vaccination, which may, therefore, have another outcome (less cost-effective) than in other countries. Another relevant issue in the decision-making process regarding introduction of universal childhood varicella vaccination in the Netherlands is the rather low reported intention to vaccinate against varicella by parents [18] and [19]. Furthermore, the effect of childhood varicella vaccination on the incidence of herpes zoster (an increase has been predicted by modelling [20]) in the Netherlands is uncertain.

Pierik et al. also identified probable varicella patients based on the ICPC-code A72 and free text in the medical journal to avoid potential under detection of varicella, and they also reviewed the medical records of all potential cases [9]. According to their study, the annual overall incidence of GP consultation due to varicella in 2004–2008 was 515 per 100,000 (standardised to the Dutch population) but when only ICPC coded diagnoses were included, the annual overall incidence was 377 per 100,000. These estimates of Pierik et al. are higher than our *maximum* IPCI estimates. A possible explanation could be differences in population characteristics (ethnicity, socio-economic factors) between IPCI and “Zorggroep Almere”. From the PIENTER 2 study, it is known that the age of infection is higher among people with a non-Dutch ethnicity [7] and [21] and in the city Almere the percentages immigrants (38%) and in particular non-western immigrants (28%) are considerably higher than in the total Dutch population (21% and 12% respectively) [22]. Pierik et al. did not provide information on hospital admission separately, but calculated the incidence (8.6 per 100,000 in the period 2004–2008) of consultations for varicella in hospital

care in general, including consultation of a specialist [9]. IPCI data showed that the standardised IR of patients having contact with hospital care due to varicella (either hospital admission or a consultation with an emergency department or a specialist) is with 6.8 (5.1–9.0) per 100,000 person-years in the same order of magnitude. In Belgium, the incidence of GP consultation due to varicella was recently estimated to be 346 per 100,000 [23], which is more in line with our estimates, while the incidence of hospitalisation due to varicella was estimated to be higher (5.3 per 100,000) [23].

There are several strengths and limitations to this study. Based on the above mentioned estimates, we may conclude that free text field searches are important for estimating the incidence of varicella in primary care data because a considerable amount of varicella patients did not receive the ICPC-code A72 as diagnosis. This was also seen by Pierik et al. [9]. Besides a free text field search, another strength of this study, is that all potential varicella cases were reviewed manually although this is labour intensive. We were not able to subtract the person-years of patients that already had varicella before 2006 (this information was only sporadically available in the medical record) and were not susceptible anymore. Therefore, the incidence was underestimated, especially in the oldest age groups [24]. However, the incidence based on the routine surveillance data has been calculated in the same way and is also comparable. Another limitation of this study design is that the information in the medical records is not always very detailed, so it was sometimes difficult to judge if a patient visited the GP because of varicella (or for another complaint which happened to coincide with the varicella episode), if a certain complication was caused by varicella and if the consultation took place at the GP practice or by telephone. This is the reason why we added the additional category “probable varicella cases” so that we were able to calculate more conservative *minimum* and *maximum* incidence estimates. The results of this study indicate that the severity of varicella among probable varicella cases was lower than among varicella cases. The differences between the *maximum* IPCI estimate and routine surveillance data with regard to the incidence of GP consultations may be explained by the fact that the routine surveillance estimates are based on ICPC coded diagnoses only (as there is no additional search in the free text fields of the medical journals like for IPCI) and patients that only consulted the GP by telephone were mostly not included. Furthermore, the GPs from routine surveillance are instructed to use the ICPC-code and have key areas of interest whereas IPCI collects all data from the GPs (coded and non-coded) without asking for monitoring of specific diseases. Moreover, at the time of our study, data could not be extracted for more recent years than the years 2006–2008. However, we expect that our data still reflect the current situation since there have been no changes in varicella vaccination policy in the Netherlands. Finally, it is possible that we missed some patients in our free text field search due to typing errors in the medical records.

To conclude, this study confirms the relatively low varicella-related consultations rate in the Netherlands, that might be linked to more conservative GP consultation behaviour in the Netherlands, and the relatively young age of infection. The results of this study will provide input for future cost-effectiveness analyses and are relevant for the decision-making process whether or not to introduce universal childhood varicella vaccination in the Netherlands.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

AUTHOR'S CONTRIBUTIONS

HdM and AvL were responsible for the design of the study; AvL coordinated the IPCI fieldwork, analysed the data and drafted the manuscript; JvE conducted most of the IPCI fieldwork during her internship; NvdM assisted in reviewing varicella complications and medication within IPCI; GD supervised data collection in the Dutch Sentinel GP Network and instructed the GPs in ICPC coding; GD, MS and HdM critically revised the manuscript. All authors read and approved the final manuscript.

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APPENDIX 1.

This appendix describes the available routine surveillance data in appendthe Netherlands regarding general practitioner (GP) consultations and hospitalisations due to varicella in the period 2006–2008. The different overall age-sex standardised IRs for varicella cases consulting a GP and for hospitalised varicella cases based on the Integrated Primary Care Information (IPCI) database and on routine surveillance data are both presented in Table A1.

[TABLE A1]

Standardised incidence rates (IR) of general practitioner consultations and hospitalisations due to varicella per 100,000 by calendar year in IPCI compared to the routine surveillance data (SENTINEL/LINH and LMR).

	General practitioner consultations				Hospitalisations		
	IPCI minimum	IPCI maximum	SENTINEL	LINH	IPCI	LMR minimum	LMR maximum
Year	IR (95%CI)	IR (95%CI)	IR	IR	IR (95%CI)	IR	IR
2006	351 (318–388)	411 (375–451)	300	260	2.7 (0.9–8.4)	1.9	2.8
2007	268 (246–292)	320 (296–346)	210	230	1.9 (0.7–5.2)	1.4	2.1
2008	266 (250–284)	355 (336–376)	290		1.8 (0.9–3.8)	1.7	2.4
Overall	281 (268–294)	354 (340–369)	267[a]		2.0 (1.2–3.4)	1.7	2.4

IPCI = Integrated Primary Care Information; SENTINEL = Dutch Sentinel General Practice Network; LINH = Dutch primary care database; IPCI minimum = estimate based on the number of varicella cases; IPCI maximum = estimate based on the sum of the number of varicella cases and probable varicella cases; LMR minimum = estimate based on the number of discharges with main diagnosis varicella; LMR maximum = estimate based on the number of discharges with main and/or side diagnosis varicella.

a

For 2006 and 2007 SENTINEL data were used. Starting in 2008, the SENTINEL has changed from registration on paper to electronic reporting, which may have resulted in underreporting of the weekly number of varicella patients. Therefore, we used data

for varicella surveillance based on ICPC codes in electronic medical records (EMRs) from LINH and sentinel general practices combined from 2008 onwards.

A.1. Dutch primary care database

Within the Sentinel GP Network, which started in 1970, GPs report on a weekly (or annual) basis on the occurrence of diseases, events and treatments that lack in routine registrations. Varicella was reported since the year 2000 until 2010. The network is representative for the total Dutch national population (with a coverage of approximately 0.7% of the population). The LINH is a network of 84 general practices with electronic patient records that collect data on the occurrence of diseases, contacts, treatments and referrals on a continuous basis. This network is also representative for the total Dutch national population.
In these networks, which are both part of the Dutch Primary Care database, the diagnoses are coded by the International Classification of Primary Care (ICPC). All patients with varicella (=ICPC-code A72) were selected; there was no additional search within free text fields. Incidence rates (IR) were calculated by dividing the total number of varicella cases by the total number of person-years within the study population. SENTINEL data were used for the years 2006 and 2007. For 2008 we used data for varicella surveillance based on LINH and SENTINEL combined. This was done because starting in 2008, the Sentinel GP Network has changed from registration on paper to electronic reporting, which may have resulted in underreporting of the weekly number of varicella patients. The estimates of the IR of GP visits due to varicella based on Sentinel/LINH were also standardised by sex and age to the total Dutch population [25] and [26].

A.2. National medical register (LMR)

This national register, which started in 1964, includes discharge diagnoses of almost all hospitals in the Netherlands. The discharge diagnoses are coded according to the International Classification of Diseases (ICD).
LMR data were used for the total period of 2006–2008 [27]. All cases with varicella (=ICD-9 code 052 or ICD-10 code B01) were selected. A *minimum* IR was calculated based on the number of discharges with main diagnosis varicella divided by the total Dutch population, a *maximum* IR was based on the number of discharges with main and/or side diagnosis varicella divided by the total Dutch population. We decided to include varicella side diagnoses in our maximum IR estimate because previous medical record research showed that approximately one quarter of varicella side diagnoses in the LMR concerned admissions that were primarily due to varicella [8]. The IR might be somewhat underestimated because not all Dutch hospitals participate each year in the LMR: because the denominator per hospital is unknown, we had to calculate the IR based on the total Dutch population.

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TABLES AND FIGURES

TABLE 1.

Medical characteristics of varicella cases and probable varicella cases in the period 2006–2008 in the Integrated Primary Care Information (IPCI) database.

Medical characteristics	Varicella cases = IPCI minimum		Probable varicella cases		Total = IPCI maximum		*p*-value [c]
	N **(N consultations)**	**%**	***N*** **(N consultations)**	**%**	***N*** **(N consultations)**	**%**	
Total	1881	100.0	467	100.0	2348	100.0	
ICPC-code A72							
No	538	28.6	278	59.5	816	34.8	
Yes, as diagnosis code	1252	66.6	172	36.8	1424	60.6	**<0.0001**
Yes, at another place in journal	91	4.8	17	3.6	108	4.6	
Type of consult[b]							
Consultation at GP practice	1585 (1969)	84.3	306 (335)	65.5	1891 (2304)	80.5	**<0.0001**
Telephone	363 (418)	19.3	148 (154)	31.7	511 (572)	21.8	**<0.00**

Medical characteristics	Varicella cases = IPCI minimum		Probable varicella cases		Total = IPCI maximum		*p*-value [c]
	N (N consultations)	%	*N* (N consultations)	%	*N* (N consultations)	%	
consultation							**01**
GP visit at home	7 (8)	0.4	–	–	7 (8)	0.3	0.357
Consultation at central GP point[a]	192 (210)	10.2	42 (44)	9.0	234 (254)	10.0	0.490
Complications							
No	1431	76.1	414	88.7	1845	78.6	**<0.0001**
Yes	450	23.9	53	11.3	503	21.4	
Prescription of medication							
No	819	43.6	269	57.6	1088	46.4	**<0.0001**
Yes	1061	56.4	198	42.4	1259	53.6	
Referral to secondary healthcare[b]							
None	1834	97.5	467	100.0	2301	98.0	**<0.001**
Specialist	27	1.4	–	–	27	1.1	**0.006**
Emergency department	17	0.9	–	–	17	0.7	0.033
Hospital admission	14	0.7	–	–	14	0.6	0.087

A Outside normal working hours of own GP practice.
B Percentages add up to more than 100% because a case can be within multiple categories.
C Pearson's χ^2 or Fisher's exact test; *p*-values in bold indicate results that are considered statistically significant after correction for multiple testing by the Benjamini–Hochberg method at a false discovery rate of 0.05.

[TABLE 2]

Comparison of diagnosis based on manual validation with diagnosis based on ICPC-code.

Diagnosis based on manual validation	Diagnosis based on ICPC-code		
	Varicella (ICPC-code = A72)	**No varicella (other ICPC-code)**	**Total**
Varicella	1343	538	1881
Probable varicella	189	278	467
Herpes zoster	7	78	85
Contact with (probably) varicella but no symptoms himself	7	163	170
Unclear if diagnosis was varicella	26	223	249
Other, not varicella related	189	684	873
Total	1761	1964	3725

Highlighted in grey: If we would have selected varicella cases based on the ICPC-code only, we would have missed 816 (probable) varicella cases that were linked to another ICPC-code (top right) and we would have included 229 additional cases that were rejected as varicella cases after manual validation (bottom left).

[TABLE 3]

Absolute number of people using healthcare due to varicella and crude and standardised incidence rates (IR) per 100,000 person-years by calendar year in the Integrated Primary Care Information (IPCI) database.

Year	General practitioner consultation				Referral to specialist		Contact with emergency department		Hospitalisation	
	Varicella cases = IPCI minimum		Total = IPCI maximum		*N*	IR (95%CI)	*N*	IR (95%CI)	*N*	IR (95%CI)
	N	IR (95%CI)	*N*	IR (95%CI)						
2006	389	325 (295–359)	454	380 (346–416)	6	5.0 (2.3–11.1)	2	1.7 (0.4–6.7)	3	2.5 (0.8–7.8)
2007	533	245 (225–266)	631	290 (268–313)	8	3.7 (1.8–7.3)	6	2.7 (1.2–6.1)	4	1.8 (0.7–4.9)
2008	959	240 (226–256)	1263	317 (300–335)	13	3.2 (1.9–5.6)	9	2.2 (1.2–4.3)	7	1.7 (0.8–3.7)
Overall - crude	1881	255 (244–267)	2348	319 (306–332)	27	3.6 (2.5–5.3)	17	2.3 (1.4–3.7)	14	1.9 (1.1–3.2)
Overall - standardised		281 (268–294)		354 (340–369)		3.9 (2.7–5.6)		2.5 (1.5–4.0)		2.0 (1.2–3.4)

IPCI minimum = estimate based on the number of varicella cases; IPCI maximum = estimate based on the sum of the number of varicella cases and probable varicella cases.

[TABLE 4]

Reported complications for varicella cases and probable varicella cases in the period 2006–2008 in the Integrated Primary Care Information (IPCI) database.

Reported complications[a]	**Varicella cases = IPCI minimum**		**Probable varicella cases**		**Total = IPCI maximum**		***p*-value**[b]
	N	**%**	***N***	**%**	***N***	**%**	
None	1431	76.1	414	88.7	1845	78.6	
Neurological							
Cerebellitis, ataxia	1	0.1	–	–	1	0.04	1.000
Febrile convulsion	8	0.4	1	0.2	9	0.4	1.000
Meningitis/encephalitis	2	0.1	–	–	2	0.1	1.000
Syncope	1	0.1	–	–	1	0.04	1.000
Lower respiratory tract							
Pneumonia	6	0.3	–	–	6	0.3	0.606
Bronchitis or bronchiolitis	17	0.9	–	–	17	0.7	0.033
Exacerbation of asthma/bronchial hyperactivity	9	0.5	1	0.2	10	0.4	0.697
Upper respiratory tract, ENT and eye							
Otitis media	102	5.4	16	3.4	118	5.0	0.097
Pharyngitis/tonsillitis	96	5.1	9	1.9	105	4.5	**0.002**
Conjunctivitis	37	2.0	11	2.4	48	2.0	0.585
Skin/subcutis							
Bacterial super infection of skin lesions	151	8.0	16	3.4	167	7.1	**<0.0001**
Scars	21	1.1	2	0.4	23	1.0	0.290
Exacerbation of constitutional eczema/contacteczema	16	0.9	–	–	16	0.7	0.054
Gastrointestinal tract							
Gastroenteritis	32	1.7	1	0.2	33	1.4	**0.013**
Stomatitis	3	0.2	–	–	3	0.1	1.000
(Imminent) dehydration	18	1.0	–	–	18	0.8	0.034
Other complications							
Anaemia	1	0.1	–	–	1	0.04	1.000

Reported complications[a]	Varicella cases = IPCI minimum		Probable varicella cases		Total = IPCI maximum		*p*-value[b]
	N	%	*N*	%	*N*	%	
Reactive arthritis	2	0.1	–	–	2	0.1	1.000
Allergic reaction on medication/urticaria	9	0.5	1	0.2	10	0.4	0.697
Other	5	0.3	–	–	5	0.2	1.000

A Percentages add up to more than 100% because a case can be within multiple categories.
B Pearson's χ^2 or Fisher's exact test; *p*-values in bold indicate results that are considered statistically significant after correction for multiple testing by the Benjamini–Hochberg method at a false discovery rate of 0.05.

[TABLE 5]

Reported medication for varicella cases and probable varicella cases in the period 2006–2008 in the Integrated Primary Care Information (IPCI) database.

Reported medication[a]	Varicella cases = IPCI minimum		Probable varicella cases		Total = IPCI maximum		*p*-value[b]
	N	%	*N*	%	*N*	%	
None	819	43.6	269	57.6	1088	46.4	
Skin–local (pruritus control and general skin care)	599	31.8	120	25.7	719	30.6	**0.010**
Antipyretics–systemic (fever and pain control)	224	11.9	42	9.0	266	11.3	0.086
Antimicrobials–systemic	174	9.3	22	4.7	196	8.3	**0.001**
Antimicrobials–local	148	7.9	24	5.1	172	7.3	0.047
Antihistaminics–systemic	92	4.9	15	3.2	107	4.6	0.137
Lidocaine–local	79	4.2	8	1.7	87	3.7	**0.009**
Upper respiratory tract – local (mucolytics/decongestive)	43	2.3	5	1.1	48	2.0	0.103
Corticosteroids – local	25	1.3	2	0.4	27	1.1	0.143
Other	80	4.3	10	2.1	90	3.8	0.031

a
Percentages add up to more than 100% because a case can be within multiple categories.
b

Pearson's χ^2 or Fisher's exact test; *p*-values in bold indicate results that are considered statistically significant after correction for multiple testing by the Benjamini–Hochberg method at a false discovery rate of 0.05.