Are children carrying the burden of broad spectrum antibiotics in general practice? - Prescription pattern for paediatric outpatients with respiratory tract infections in Norway

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2012-002285
Article Type:	Research
Date Submitted by the Author:	30-Oct-2012
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Primary Subject Heading:	General practice / Family practice
Secondary Subject Heading:	Paediatrics, Pharmacology and therapeutics, Respiratory medicine
Keywords:	Respiratory, General Paediatrics, Community child health < PAEDIATRICS, PRIMARY CARE

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Are children carrying the burden of broad spectrum antibiotics in general practice? *- Prescription pattern for paediatric outpatients with respiratory tract infections in Norway*

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Keywords: general practice, children, antibiotics, prescriptions, respiratory tract infections

Word count: 2600

Figures: 2

Tables: 4

Article summary

Article focus:

- Scandinavia has a conservative prescription pattern for antibiotics in respiratory tract infections.
- Norwegian guidelines recommend the use of phenoxymethylpenicillin in almost all upper respiratory tract infection in general practice.
- Specific challenges apply when prescribing drugs to children.

Key messages:

- The general prescription rate for antibiotics in respiratory tract infections is relatively low in Norway, but higher in children than adults.
- Norwegian GPs tend to over prescribe macrolide antibiotics to children.
- The national guidelines for antibiotics in general practice are not followed in children diagnosed with bronchitis/bronchiolitis.

Strengths and limitations:

- Large data set with representative GPs from different parts of Norway participating.
- Analyses done at episode level, limiting the risk of including re-visits for the same illness.
- Data mainly from 2005, however, recent data from the Norwegian Prescription Data base indicate that the presription pattern has undergone few changes since then.

Abstract

Objectives: To investigate the antibiotic prescription pattern and factors that influence the physicians' choice of antibiotic.

Design: Observational study.

Setting: Primary health care in Norway, December 2004 through November 2005.

Participants: 426 general practitioners, GPs, in Norway, giving 24 888 respiratory tract infection episodes with 19 938 children aged 0-6 years.

Outcome measures: Assess antibiotic prescription details and patient and GP characteristics associated with broad spectrum and narrow spectrum antibiotic use.

Results: Of the 24 888 episodes in the study, 26.2 % (95 % confidence interval (CI): 25.7-26.8) included an antibiotic prescription. Penicillin V accounted for 42 % and macrolide antibiotics for 30 %. The prescription rate varied among the physicians, with a mean of 25.5 % (95 % CI: 24.2-26.7). Acute tonsillitis gave the highest odds for a prescription, odds ratio (OR) 33.6 (CI: 25.7-43.9), compared to "acute respiratory tract infections and symptoms" as a reference group. GPs with a prescription rate of 33.3 % or higher, had the larger probability for broad spectrum antibiotic prescriptions, OR 3.33 (CI: 2.01-5.54). Antibiotic prescriptions increased with increasing patient age.

Conclusions: We found a low antibiotic prescription rate for childhood respiratory tract infections. However, our figures indicate an over-use of macrolide antibiotics and penicillins with extended spectrum, more so than in the corresponding study including the adult population. Palatability of antibiotic suspensions and other administrative challenges affect medication compliance in children. To help combat antibiotic resistance, guidelines need to be followed, in particular for our youngest patients.

Contributors

GF, ML and SG conceived the idea of the study and were responsible for the design of the study. GF, SG and ID were responsible for the data analyses and produced the tables and graphs. ID designed the model used for multilevel analysis. All authors provided input into the data analysis and to the interpretation of the results. The initial draft of the manuscript was prepared by GF, ML and KK and then circulated repeatedly among all authors for critical revision.

Competing interests

ICMEJ forms are submitted for all authors. S.G. is working part time and has ownership in the company that produced software for data extraction in this study. All other authors: none to declare.

Funding

The Rx-PAD study was carried out with grants from the Norwegian Ministry of Health and the Norwegian Medical Association. The present study is funded as part of a PhD-project by the Antibiotic Center for Primary Care.

Ethics approval

The Rx-PAD-study, merged with the data from NorPD was approved by the regional ethics committee, the Norwegian data inspectorate and the Norwegian Directorate of Health.

Data sharing statement

There is no additional data available.

Trial registration number (clinicaltrials.org):

NCT00272155

Introduction

Almost 90 % of antibiotics sold in Norway are prescribed in the primary health care sector [1]. The most common antibiotic subtype is phenoxymethylpenicillin, followed by erythromycin, pivmecillinam and doxycycline [2]. Although the Scandinavian prescription pattern is conservative, the European trend of increased use of broad spectrum penicillins and macrolide antibiotics is also found in Norway [2-4]. More recent figures from both Holland and the United States from 1998 to 2004 confirm the tendency [5, 6].

The use of antibiotics in Norwegian children aged 0-4 years was approximately 30 % in 2005/2006, compared to an average of about 24 % in the general population [1]. Users per 1000 aged 0-9 years were 220 in 2005 and 227 in 2011 [7]. Most prescriptions for children in primary health care are results of common airway infections. A Norwegian study from 1989 found that 80 % of general practice (GP) contacts for children aged 0-12 years with the diagnoses tonsillitis, sinusitis, acute bronchitis, bronchiolitis and pneumonia were prescribed antibiotics, with phenoxymethylpenicillin as the drug of choice [8].

When prescription rates are considered, it is important to keep in mind that several studies from general practice show that consultations for upper respiratory tract infections are decreasing, while the proportion of antibiotic prescriptions remains constant [9-12]. Variations in physician seeking behaviour and changing prescription pattern among GPs are suggested explanations. Adequate and rational use of antibiotics is one needed action to prevent and combat antibiotic resistance [13, 14], hence several surveillance systems monitor the use of antibiotics on national and European levels [15-17]. The proportion of pneumococcus airway isolates with reduced penicillin sensitivity was 3.3 % in 2007 and shows an increasing tendency [16]. Erythromycin resistance in pneumococcus airway isolates increased from 2 % in 2000 to 12.4 % in 2006 but decreased to 9.4 % in 2007 [16, 18]. Resistance to macrolide antibiotics is of particular importance in children. Studies have shown resistant strains in their oral flora in 17 % of patients six weeks following treatment with erythromycin, and 85 % for azithromycin [19].

Norwegian guidelines present phenoxymethylpenicillin as the drug of choice in almost all upper respiratory infections if antibiotics are required [20]. The level of resistance is low, and the only reasons for second-choice antibiotics are penicillin allergy or treatment failure. Compliance is an important issue when antibiotic suspensions are subscribed, palatability being one determinant [21].

The aim of the study was to investigate the prescription pattern of antibiotics for respiratory tract infections in Norwegian primary health care in pre-school children; estimate the prescription rate and assess factors affecting the GP's prescription pattern.

Material and methods

The Prescription Peer Academic Detailing (Rx-PAD) Study was initiated in 2004 at the University of Oslo to provide structured training in the use of prescription drugs for GPs. 80 GP training groups including approximately 450 physicians from different parts of the country were recruited with the purpose of raising awareness and improving GP's prescription patterns in respiratory tract infections and prescription drugs for the elderly [22]. As part of the Rx-PAD study, a one-year sampling of baseline data from 441 GPs were performed (December 2004 through November 2005); the material of the present study. All respiratory tract infection diagnoses were included, based on the International Classification of Primary Care (ICPC-2) coding system [23]. Data were extracted from the doctors' computer systems using software developed by Mediata AS.

Of the 441 GPs in the project, 12 GPs with less than 10 registered episodes, 72 episodes where patient gender was missing and three GPs in rural practices with an over-the-counter delivery of antibiotics were excluded. The total number of episodes available for analysis were 24 888, including 19 938 patients and 426 GPs (Figure 1).

The Rx-PAD database was merged with the Norwegian National Prescription Database (NorPD). Information included in the database are the drug specific anatomical therapeutic chemical (ATC) codes, name, strength, administration form, compound size and the date of withdrawal by the patient [24].

The outcome of interest for the present study was antibiotic prescription details from the GPs. The following diagnoses were included according to the ICPC-2 classification system: acute respiratory tract infections and symptoms (R01-29,74,80), acute bronchiolitis/bronchitis (R78), pneumonia (R81), acute otitis media and ear pain (H01,71,72,74), acute tonsillitis (R72,76) and other respiratory tract infections including sinusitis, laryngitis and asthma (R71, 75, 77, 79, 83, 95, 96) [23].

Consultations with pre-school children, aged 0-6 years, were extracted from the Rx-PAD baseline data to form a distinct database in SPSS. Consultations within 30 days of each other were combined to form one episode, of which the first antibiotic prescription of the episode was selected for further analysis. Analyses were performed by episode; one patient may be included more than once. Less common antibiotics were grouped. Antibiotics common for urinary tract infections and rarely in use for respiratory infections (nitrofurantoin, trimethoprim, pivmecillinam and methenamine) were coded as no antibiotic prescription.

Descriptive statistics were estimated in IBM SPSS Statistics 19. Logistic regression models were used to identify predictors of antibiotic prescription and predictors of broad-spectrum antibiotic prescription in Stata IC/11.2 for Windows. The results from logistic regression analyses were adjusted for clustering by means of multilevel modelling with random intercept at the group and doctor level, and random slope at diagnoses for doctors.

Results

GP characteristics are shown in Table 1.

Table 1: Characteristics of 426 participating GPs

Characteristic (n = 426)	Number	% [95 % Confidence interval]
Gender		
Female	135	31.7 [27.3 – 36.1]
Male	291	68.3 [63.9 – 72.7]
Group practice		
Yes	394	92.5 [90.0 – 95.0]
No	32	7.5 [5.0 – 10.0]
GP specialist		
Yes	365	85.7 [82.4 – 89.0]
No	61	14.3 [11.0 – 17.6]
Practice location		
City	233	54.7 [50.0 – 59.4]
Rural	193	45.3 [40.6 – 50.0]
	Mean	**Median [Range]**
Age (years)	49	50 [28 – 67]
Years since authorization	19	20 [0 – 41]
Number of listed patients	1 328	1 316 [0 – 3 385]
Consultations per year	3 095	3 029 [309 – 11 252]

A total of 426 GPs were included in the study, 31.5 % and 68.5 % females and males, respectively. 86 % of the physicians were authorized GP specialists. Most GPs worked in a group practice.

The prescription pattern among GPs varied considerably, with a mean of 25.5 (95% confidence interval (CI) 24.2-26.7) antibiotic prescriptions per 100 episodes. For broad spectrum antibiotic proportion, the corresponding figure was 53.7 (95% CI 50.7-56.7). Among the latter, more than 50 doctors prescribed broad spectrum antibiotics every time. (Figure 2)

Respiratory infections were most common among 2-3 year olds, 41% experienced infections, and fewer episodes were found in June, July and August. Of the 24 888 episodes, 53 % were boys and 47 % were girls. The three most common diagnoses were acute upper respiratory tract infection (R74), cough (R05) and acute otitis media (H71), 27 %, 18 % and 16 % respectively. 20 % of the episodes are repeating visits.

An antibiotic prescription was registered in 26.2 % (6 525) of all episodes. Penicillin V was prescribed most frequently, followed by macrolide/lincosamide antibiotics. In the latter group, lincosamides accounted for only 1.3 %; the group is therefore referred to as macrolides [25]. Few registered prescriptions of tetracyclines and cephalosporins for respiratory tract infections were found. Episodes with acute tonsillitis resulted in a prescription in 77 %, and more than 67 % of the prescriptions were penicillin V. As shown in Table 2, a high antibiotics rate for acute bronchitis was found, 40 %, with macrolide antibiotics as the choice of preference. When patients were diagnosed “other respiratory tract infections”, only 12 % of the episodes resulted in antibiotic prescriptions. In the latter, 52 % of the episodes resulted in macrolide antibiotics and 22 % in penicillins with extended spectrum. In the otitis media group where antibiotics were prescribed, penicillin V and penicillins with extended spectrum were provided in 46 % and 33 % respectively. A lower prescription rate was found in children below age one (n=1552), where only 10% received an antibiotic prescription.

Table 2: Antibiotic prescriptions of 426 GPs for 24 888 RTI episodes for one year (Dec 2004 through to Nov 2005) according to ICPC-2 diagnoses and type of antibiotic

Diagnoses	ICPC-2 codes	Episodes N	Prescription rate (%) [95 % CI]	PcV n (%)	Pc-Ext n (%)	Mac n (%)	Other J01 n (%)
Acute upper respiratory tract infections & symptoms	R01-29, 74, 80	6806	13.5 [12.7-14.3]	388 (42)	245 (27)	272 (30)	17 (2)
Other respiratory tract infections (incl. sinusitis, laryngitis)	R71, 75, 77, 79, 83, 95	8758	12.4 [11.7-13.1]	271 (25)	236 (22)	562 (52)	17 (2)
Acute bronchiolitis/bronchitis	R78	1481	40.2 [37.7-42.7]	141 (24)	138 (23)	309 (52)	8 (1)
Pneumonia	R81	606	67.0 [63.3-70.7]	127 (31)	97 (24)	178 (44)	4 (1)
Acute otitis and ear pain	H01, 71, 72, 74	5961	42.5 [41.2-43.8]	1174 (46)	832 (33)	477 (19)	53 (2)
Acute tonsillitis	R72, 76	1276	76.7 [74.4-79.0]	654 (67)	137 (14)	176 (18)	12 (1)
Total		24888	26.2 [25.7-26.7]	2755 (42)	1685 (26)	1974 (30)	111 (2)

PcV = Penicillin V
PcExt = Penicillins with extended spectrum (non-penicillin V)
Mac = Macrolide and lincosamide antibotics
Other J01 = Cephalosporins, co-trimoxazole and tetracyclins

Predictors for antibiotic prescriptions are shown in table 3. Tonsillitis and pneumonia gave the highest odds ratio for antibiotics among the diagnostic groups, with odds ratios (ORs) of 33.6 (CI 25.7-43.9) and 16.5 (CI 12.7-21.4) respectively. Older children had an increased probability for antibiotics compared to the age group 0-1 years (Table 3). Gender or GP characteristics did not predict antibiotic prescriptions, except for GPs with a high work load (measured by annual consultations), which were more frequent prescribers. Bivariate analysis found increased ORs for antibiotic prescriptions among GPs in single practice and non-specialists, but these differences did not remain significant after adjustment.

Table 3: Multiple logistic regression analysis showing factors independently associated with 426 GPs' antibiotic prescriptions for 24 888 RTI episodes during one year (Dec 2004 through to Nov 2005)

Patient factors	**n (episodes)**	**Adj odds ratio (95% CI)**
Patient's gender		
• Male (ref)	13 214	1
• Female	11 674	0.97 (0.90-1.04)
Group of diagnoses		
• Acute upper respiratory tract infections & symptoms (ref)	6 806	1
• Other respiratory tract infections	8 758	**0.76 (0.67-0.87)**
• Acute bronchitis	1 481	**4.35 (3.53-5.35)**
• Pneumonia	606	**16.5 (12.7-21.4)**
• Acute otitis & ear pain	5 961	**5.16 (4.55-5.85)**
• Acute tonsillitis	1 276	**33.6 (25.7-43.9)**
Patient age		
• <2 yrs (ref)	7 909	1
• 3-4 yrs	10 118	**1.34 (1.24-1.46)**
• 5-6 yrs	6 861	**1.41 (1.28-1.54)**
Doctor factors		
Doctor's gender		
• Male (ref)	16 281	1
• Female	8 607	1.06 (0.88-1.28)
Practice location		
• City (ref)	14 009	1
• Rural	10 879	1.00 (0.84-1.18)
Practice type		
• Group (ref)	23 207	1
• Single	1 681	1.10 (0.81-1.49)
Educational level		
• GP specialist (ref)	21 798	1
• Not specialist	3 090	**1.38 (1.06-1.81)**
Doctor's age		
• 28-43 (ref)	7 096	1
• 44-49	7 544	1.19 (0.94-1.52)
• 50-54	5 833	1.05 (0.82-1.36)
• 55-67	4 415	1.12 (0.86-1.44)
Patient contacts per year		
• 309-2302 (ref)	4 025	1
• 2303-3028	5 495	1.16 (0.91-1.47)
• 3029-3711	7 060	1.27 (0.99-1.62)
• 3712-11252	8 308	**1.54 (1.20-1.97)**

Regression analysis on predictors for broad spectrum antibiotics showed a similar pattern (Table 4). The diagnoses giving the highest odds ratios were the group of other respiratory infections and bronchitis, ORs of 3.04 (CI 2.28-4.05) and 2.71 (CI 1.91-3.86) respectively gave the highest odds ratios compared to the reference group of acute respiratory tract infections. The probability for broad spectrum antibiotics was low for tonsillitis, and increasing age lowered the probability (Table 4). Predictors of broad spectrum antibiotics with regards to the GP gave higher odds ratios for specialist GPs. The most significantly increased odds ratio was seen in high prescribers, OR 3.33 (CI 2.01-5.54), for GPs with prescription rates of 33.3-77.8 %.

Table 4: Multiple logistic regression analysis showing factors independently associated with 426 GPs' proportion of broad spectrum antibiotics (non-Penicillin V) for 6 525 RTI episodes with prescribed antibiotic for one year (Dec 2004 through to Nov 2005)

Patient factors	**n (episodes)**	**Adj odds ratio (95% CI)**
Patient's gender		
• Male (ref)	3 490	1
• Female	3 035	1.04 (0.91-1.19)
Group of diagnoses		
• Acute upper respiratory tract infections & symptoms (ref)	922	1
• Other respiratory tract infections	1 086	**3.04 (2.28-4.05)**
• Acute bronchitis	596	**2.71 (1.91-3.86)**
• Pneumonia	406	**2.10 (1.46-3.02)**
• Acute otitis & ear pain	2 536	1.11 (0.87-1.43)
• Acute tonsillitis	979	**0.24 (0.18-0.33)**
Patient age		
• <2 yrs (ref)	1 533	1
• 3-4 yrs	2 888	1.13 (0.94-1.35)
• 5-6 yrs	2 104	**0.79 (0.66-0.96)**
Doctor factors		
Doctor's gender		
• Male (ref)	4 310	1
• Female	2 215	0.83 (0.56-1.24)
Practice location		
• City (ref)	3 689	1
• Rural	2 836	1.07 (0.72-1.59)
Practice type		
• Group (ref)	6 038	1
• Single	487	1.21 (0.61-2.34)
Educational level		
• GP specialist (ref)	5 658	1
• Not specialist	867	**0.53 (0.30-0.94)**
Doctor's age		
• 28-43 (ref)	1 878	1
• 44-49	1 927	0.71 (0.43-1.19)
• 50-54	1 489	1.06 (0.62-1.80)
• 55-67	1 231	0.85 (0.49-1.49)
Patient contacts per year		
• 309-2302 (ref)	955	1
• 2303-3028	1 367	1.48 (0.90-2.44)
• 3029-3711	1 889	1.23 (0.74-2.06)
• 3712-11252	2 314	1.44 (0.85-2.46)
Antibiotic prescription rate(%)		
• 0-15.60 (ref)	580	1
• 15.61-23.64	1 236	1.15 (0.69-1.90)
• 23.65-33.33	1 942	1.37 (0.84-2.23)
• 33.34-77.78	2 767	**3.33 (2.01-5.54)**

Discussion

Our results showed frequent use of broad spectrum antibiotics for RTIs in children, but a low overall prescription rate. Over-prescription was found for bronchitis and in busy GPs.

Although Penicillin V was the most frequent preferred choice of antibiotic in 42 % of childhood diagnoses, a high percentage of broader spectrum antibiotics, especially macrolides, was found. An overall 30 % macrolide use is seen in the present study. A proportion of 52 % for bronchitis differs from a bronchitis macrolide proportion of 32 % in the corresponding study where adult data also are included [26]. The use of penicillin with extended spectrum is recommended prior to the use of macrolides due to resistance issues [16, 18, 19]. Macrolides, according to the Norwegian guidelines for antibiotic use in primary care [20, 27], are first choice of preference only in suspected atypical pneumonia or penicillin allergy. In our study they have been used for other diagnoses as well. One explanation may, at least in part, be administrative convenience and a more preferential taste compared to the bitter-tasting Penicillin V. It has been found that tolerability, taste and administrative frequency are of importance in paediatric populations [21, 28, 29]. When Hoppe and co-workers tested paediatric compliance in oral antibiotics, a compliance of 94 % and 90% was found for clarithromycin and erythromycin. Correspondingly, penicillin V suspensions had a compliance rate of 62 and 56 % [30]. Hinnerskov et al have highlighted a similar problem of macrolide overuse in Denmark [31].

The overall prescription rate of only 26 % for RTIs in children aged 0-6 years in our study was rather low compared to the corresponding data including the adult population [26]. Although a low rate in pre-school children of 24 % was found of the latter, a high proportion was broad spectrum antibiotics [26]. Blix et al reported population prevalence for all antibiotic prescriptions of 24 % and for children 0-4 years about 30 % in 2005/2006 [1]. Our selection only included RTIs, and is, accordingly, somewhat lower. Compared to a Norwegian study from 1998 [8], a prescription rate of only 26 % shows a decreasing tendency. In 1998, antibiotics was the rule rather than the exception for children visiting GPs for otitis media, tonsillitis, sinusitis, bronchitis/bronchiolitis and pneumonia [8].

Antibiotic prescriptions by diagnosis showed a similar distribution pattern to that of the corresponding dataset including adults, but a higher rate for otitis media and a lower rate for symptom diagnoses and bronchitis [26]. Substantial effort has been performed in Norway the past decade to decrease the prescription rate of antibiotics. Our data indicate that these efforts are about to pay off. For instance, we found a low antibiotic prescription rate in patients with otitis media, 42.5 %. This is in accordance with current Norwegian guidelines [20]. Comparable figures from previous studies on antibiotic prescriptions for RTIs in children in several countries revealed an average prescription rate of 47 %. Among the 14 study populations included in the study, Italy and Canada have high levels of 42 and 57 % respectively. Holland and UK correspondingly low levels of 14 and 21 % [32].

Predictors of antibiotic prescriptions

The prescription rate of 40 % for bronchitis/bronchiolitis was worryingly high. This figure is lower than the former study from 1998 [8], but not in correspondence with current Norwegian guidelines [20]. Considerable improvement in prescription routines is needed. Cochrane reviews have shown no evidence for treating acute bronchiolitis in children with antibiotics, and only a modest beneficial effect when treating patients 8 to 65 [33, 34]. No obvious explanation to the high prescription rate for bronchitis is evident, but one reason may be a perceived patient or parental demand for prescription, as reported by Little et al. in 2004 [35]. We also suspect that some diagnoses may be registered based on symptom findings, although the GP suspected more serious illness and subsequently prescribed antibiotics. C-reactive protein, CRP-testing, is usually performed following clinical examination, and after the ICPC-2 coding. Elevated CRP may cause a prescription without a corresponding change in the initial ICPC-2 code. In the present study, 12-14 % received antibiotics based on symptom diagnoses only. Jansen et al report similar results from Holland, with a symptom diagnose prescription rate of 12-15 % for pre-school children [36]. Such infections are likely to have viral pathology. A correspondingly low prescription rate is expected.

Children aged 5-6 years had the highest probability for antibiotic prescriptions, children below age two the lowest. An opposite pattern was seen in the prescription pattern for broad spectrum antibiotics. Another factor influencing antibiotic prescription was related to GP experience, as GP non-specialists were more likely to prescribe antibiotics. A high number of patient contacts per year increased prescription likelihood. High antibiotic prescription rates increased the probability for broad spectrum antibiotics. Slightly surprising, GP specialists tend to use more broad spectrum antibiotics than those without the specialist authorization. Similar results are presented by Clavenna et al, suggesting physician attitude may play a role obtaining prudent antibiotic prescriptions [37]. Antibiotic overuse may also be affected by an existing gap between perceived and real determinants of antibiotic prescription [38].

<u>Strengths and limitations</u>

The major strength of this study is the large number of infectious episodes in the data set. The study period comprised a complete year, including all seasonal variations. GPs from most parts of the Southern Norway participated; urban as well as rural areas. We believe it is likely that our data represents the prescription pattern for respiratory tract infections well and that our findings are generalizable to Norwegian GPs. We have chosen to analyse by infectious episodes, with a cut off at 30 days, well aware that a few new episodes may represent re-visits due to treatment failure and follow-up visits by the same patient. Previous studies have been performed based on consultations and by infectious episodes [32, 36]. The consultations in the present study only represent GPs' regular office work, no out-of-hour emergency visits are included. In most of Norway, the same office GPs also are on duty taking care of emergency cases during evenings and nights. A study by Fagan et al from 2008 showed that Norwegian GPs' prescription patterns are identical when regular office consultations are compared to emergency visits for otitis media and tonsillitis [39]. Our data are mainly from 2005, however figures from NorPD indicate similar patterns of antibiotic use now in 2011 [7].

In conclusion, a low antibiotic prescription rate for childhood respiratory tract infections was found. However, the GPs tend to choose macrolide antibiotics and penicillins with extended spectrum more often than the guidelines recommend. We recognise the specific challenges that are related to medication compliance in children. Administrative simplifications, such as the availability to oral penicillin suspensions during meals, may help shift the trend away from broad spectrum antibiotics [40]. Palatability may also affect compliance, taking Penicillin V's bitter taste into account. Differences between GPs can be targeted by more individual and specified means. We recommend that GPs replace narrow spectered penicillins with extended spectered penicillins rather than macrolides as second choice antibiotic in RTIs.

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STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract **Page 2 (abstract)**
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found **Abstract, page 2 and Summary, page 21**
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses **Introduction, pages 4 and 5**
Methods		
Study design	4	Present key elements of study design early in the paper **Page 6**
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection **Pages 6, 7 (figure) and 8**
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants **Page 7 (figure) and 8**
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable **Page 8**
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group **Page 8**
Bias	9	Describe any efforts to address potential sources of bias **Pages 7 (figure) and 8**
Study size	10	Explain how the study size was arrived at **Figure at page 7**
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why **Page 8**
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions

(*c*) Explain how missing data were addressed

Figure at page 7, statistical methods at page 8

(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed

Case-control study—If applicable, explain how matching of cases and controls was addressed

Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy

Results, pages 10-16

(*e*) Describe any sensitivity analyses

Continued on next page

Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram **Figure at page 7, tabel 1 at page 9**
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders **Table 1 at page 9 (also Figure 1 at page 7)**
		(b) Indicate number of participants with missing data for each variable of interest **Figure 1 (page 7)**
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures **Figure 1 (page 7), page 8, Table 1 (page 9)**
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included **Results, pages 9-16 incl figures and tables**
		(*b*) Report category boundaries when continuous variables were categorized **Table 3 (page 14), Table 4 (page 16)**
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives **Disussion, pages 17-20, and Summary, page 21**
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias **Page 19**
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence **Page 19-20**
Generalisability	21	Discuss the generalisability (external validity) of the study results **Page 19-20**
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based **Page 3**

Figure 1: Selection process after data from 441 GPs and 25 093 RTI episodes for one year (December 2004 through to November 2005) were collected

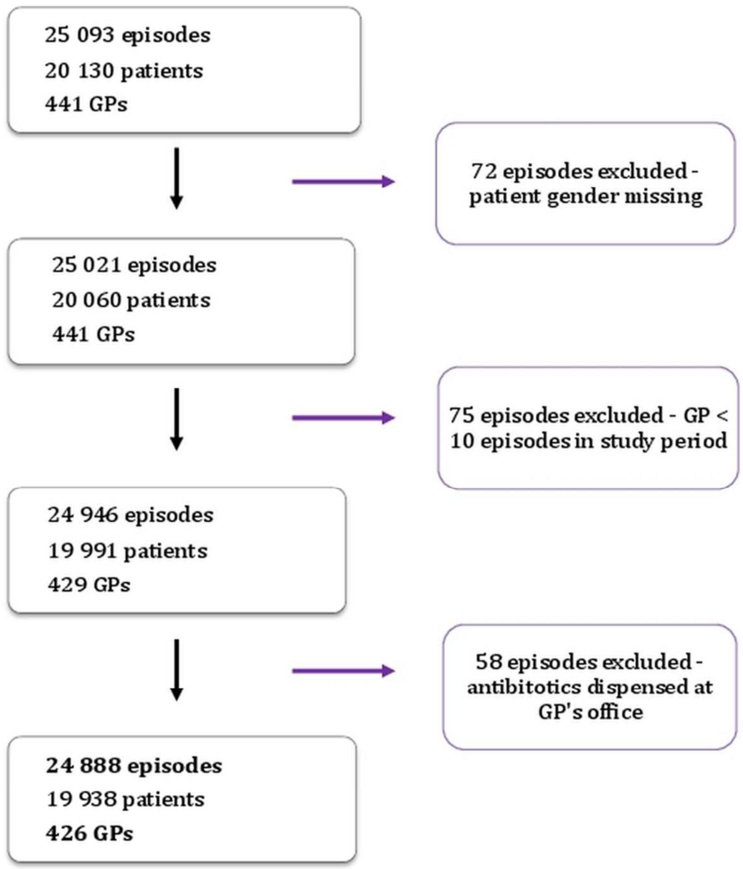

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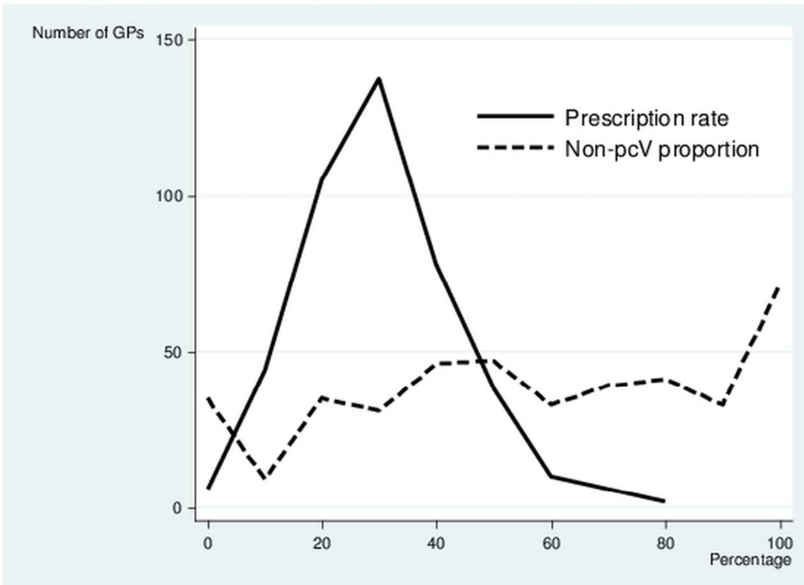
Figure 2: Antibiotic prescription rates for RTI episodes and proportion broad spectrum antibiotic prescriptions among the 426 participating GPs



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