

Antibiotic prescribing for respiratory tract infections in Dutch primary care in relation to patient age and clinical entities

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Objectives: To obtain detailed information on current prescribing rates of antibiotics for respiratory tract infections (RTIs) in Dutch general practice and its relation with age and respiratory tract clinical entities.

Methods: We assessed the mean proportion of antibiotics prescribed for RTIs per age group, contact-based and population-based using all patient contacts concerning RTIs in the year 2000 selected from the IPCI database, containing information on general practice consultations of 235 290 patients.

Results: In one-third of all contacts concerning RTIs, antibiotics were prescribed, with much variation between age groups and clinical entities. For children (0–15 years) and the elderly (over 75 years), the lowest contact-based percentages of prescribed antibiotics for RTIs were found, while population-based, children of age 0–5 years received far more antibiotics for RTIs. High prescribing rates were seen in patients with sinusitis-like complaints (67%) or pneumonia (78%), whereas low rates were found for patients with upper RTIs (16%).

Conclusions: Potential over-prescribing of antibiotics for RTIs occurs in the age group 31–65 years, not in children and the elderly, and in patients with upper RTIs, sinusitis and most likely acute bronchitis (contact-based). The management of these subgroups of patients should be addressed in quality assurance programmes. Children and the elderly visit the GP much more often than adults, which can be explained by more frequent (children) or more severe (elderly) RTI morbidity, but in proportion they do not receive more antibiotics.

Keywords: antibiotic prescriptions, respiratory tract infections, age, the Netherlands

Introduction

About two-thirds of antibiotic prescriptions in general practice are for respiratory tract infections (RTIs).¹ Over the last decade, general practitioners (GPs) have been encouraged to prescribe more rationally and to follow evidence-based guidelines when prescribing antibiotics.² However, implementation of guidelines in this field has proven to be difficult.³ Quality assurance programmes are needed to enhance rational antibiotic use. To tailor such activities to relevant issues in this field, detailed

information on current antibiotic prescribing for RTIs, including patient age, is needed.

Population-based studies in the Netherlands as well as in the UK found that antibiotic prescribing rates are highest in children aged 0–4 years and in the elderly (over 75 years).^{4,5} High antibiotic prescribing rates are especially seen in children with RTIs, despite recommendations not to prescribe antibiotics for such indications.⁶

The purpose of this study was to obtain detailed information on current prescribing rates of antibiotics for RTIs in Dutch

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Table 1. International Classification of Primary Care codes with free text words for symptoms and diagnoses per respiratory tract clinical entity

Clinical entity	Symptoms	Diagnoses
		Upper respiratory tract
Ear	H01: earache/ear pain H02: hearing complaints H04: discharge/blood from ear H29: other symptoms/complaints of ear	H71: acute otitis media H72: serous otitis media H73: eustachian salpingitis H74: chronic otitis media H77: perforation tympanic membrane
Upper respiratory tract	R07: sneezing/nasal congestion R08: other symptoms of nose	R74: upper respiratory infection/head cold R83: other infections respiratory system
Sinus	R09: symptoms/complaints sinus	R75: sinusitis acute/chronic
Throat	R21: symptoms/complaints throat R22: symptoms/complaints tonsils	R76: tonsillitis acute R77: acute laryngitis/tracheitis/croup R90: hypertrophy/chronic infect tonsils
		Lower respiratory tract
Pneumonia		R81: pneumonia
Cough/bronchitis	R01: pain attributed to respiratory system R02: dyspnoea R03: wheezing R05: cough R25: abnormal sputum/phlegm	R71: whooping cough R72: strep-throat/scarlet fever R78: acute bronchitis/bronchiolitis R79 or R91: chronic bronchitis

general practice and examine its relation with age and respiratory tract clinical entities.

Materials and methods

Data for this study were retrieved from the Integrated Primary Care Information (IPCI) database. This database, maintained by the Department of Medical Informatics at the Erasmus MC—University Medical Center Rotterdam in the Netherlands, is a longitudinal observational GP research database that contains data from computer-based patient records from about 80 GP practices throughout the Netherlands. In the Netherlands, inhabitants are registered with a single GP, who acts as a gatekeeper to secondary care. GPs participating in the IPCI project are fully automated. Hence, records from each GP can be assumed complete for an individual patient. As of January 2000, 150 GPs were providing data to the IPCI database on an ongoing basis. The number of patients in 2000 amounted to 235 290. The database contains information on patient demographics (age, gender, insurance type), symptoms and diagnoses [in free text and using the International Classification of Primary Care (ICPC) codes⁷], medication prescriptions [coded according to the Anatomical Therapeutic Chemical (ATC) classification⁸], indications for therapy, referrals and specialist letters. The system complies with European Union guidelines on the use of medical data for research.⁹

The study period encompassed the year 2000. Our source population comprised all patients who were registered in the year 2000 with one of the participating GPs. Patients from GPs who provided data only for a part of the year 2000 were excluded. From this population, we selected all patients with at least one RTI as diagnosed by the GP in the year 2000. We used a stepwise approach to select all patient records related to an RTI during the study period. Eligible patient records included surgery encounters, home visits and telephone contacts.

In a first step, a sensitive search strategy was carried out in patients' medical notes and problem lists (lists of main medical problems of the patient, which the GP wants to be aware of during any

patient encounter) to identify all records pertaining to RTI. This search included all relevant ICPC codes and related free text words, which were specified for each clinical entity (Table 1).

In a second step irrelevant records, such as specialist letters and negations of the free text word (e.g. no, not, never), were excluded. If a contact was selected because of a free text word only, and this contact also included an ICPC code which was not related to the specific respiratory tract clinical entity, this contact was excluded, because the RTI was assumed to be a secondary health problem. In the case of two RTI ICPC codes or two RTI free text words (in most cases both a symptom and a diagnosis), the contact was categorized as a diagnosis.

RTI contacts were described by patient characteristics (gender, age, insurance type), type of contact and antibiotic medication (ATC codes starting with J01) prescribed during the contact. All RTI contacts were categorized into clinical entities (ear, upper respiratory tract, sinus, throat, pneumonia, and cough/bronchitis), and were classified as symptoms or as diagnoses (Table 1).

Analysis

Antibiotic prescribing was calculated as the number of RTI-related contacts in which antibiotics were prescribed divided by the number of RTI-related contacts in an age group (contact-based). In addition, we divided the number of patients per age group in whom an antibiotic was prescribed for an RTI by the total number of patients in that age group (population-based). Furthermore, we calculated the mean number of RTI contacts in the year 2000 per 5-year age groups; 5 year age groups were used because of comparability with literature. We determined the age groups on 1 July 2000. Subsequently, we calculated the mean contact-based antibiotic use in four age groups per RTI clinical entity. Age groups in this calculation were classified as pre-school children (0–4 years), school children (5–12 years), adolescents and adults (13–64 years) and elderly (65+ years). This was done because GPs frequently use this classification, in which every age group has its specific RTIs. Age

below 12 years for example is a contra-indication for some antibiotics. χ^2 statistics were used to compare antibiotic prescribing rates between categories.

Results

The study population consisted of 42 726 patients with at least one contact concerning RTIs in the year 2000 (18% of all patients in the year 2000). In all, there were 64 735 RTI contacts, resulting in a mean of 1.5 (s.d. 1.0) contacts per patient. Sixty-one percent of all relevant contacts had an ICPC code for RTI, the remaining being based on free text words. Most patients were female (56%) and mean age of the patients was 33 years (range: 0–102) (Table 2). Most of the contacts were surgery encounters (82%), 8% were telephone contacts and 5% were home visits. In 5% the type of contact was not specified.

Overall, antibiotics were prescribed in almost one-third of all RTI contacts (31%, Table 3). The lowest contact-based percentages of antibiotics prescribed were found in children (0–15 years) and in the elderly (over 75 years) (Figure 1), who both

Table 2. Characteristics of patients with at least one respiratory tract infection contact in the year 2000

Patient characteristics (n = 42 726)		Number (%)
Gender	male	18 796 (44)
	female	23 930 (56)
Age	0–4 years	6811 (16)
	5–12 years	3836 (9)
	13–64 years	26 300 (62)
	over 65 years	5779 (13)
Insurance type ^a	sickness fund	26 689 (62)
	private	14 775 (35)

^aMissing, 1262 (3%).

Table 3. Antibiotic prescribing rates in respiratory tract clinical entities in the year 2000 (contact-based)

	Number of RTI contacts	Number of antibiotic prescriptions [antibiotic prescribing rate (%)]
Diagnoses	35 673	16 256 (46)
Symptoms	29 062	3854 (13)
Ear	6536	2131 (33)
Upper respiratory tract	13 072	2092 (16)
Sinus	7284	4875 (67)
Throat	11 156	3645 (33)
Pneumonia	1043	811 (78)
Cough/bronchitis	25 644	6556 (26)
Gender		
male	28 236	8718 (31)
female	36 499	11 392 (31)
Insurance type		
sickness fund	40 759	12 327 (30)
private	21 918	7007 (32)
Total/mean	64 735	20 110 (31)

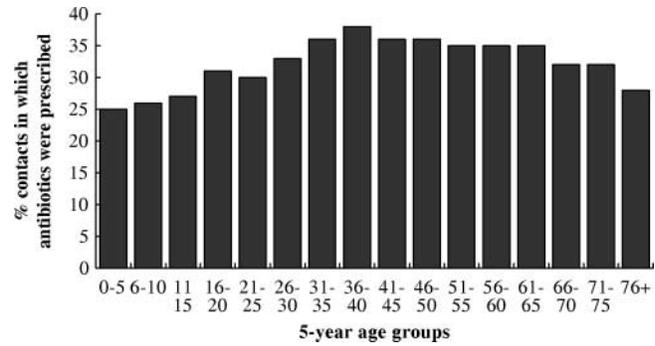


Figure 1. Percentage of respiratory tract infection contacts in which antibiotics were prescribed, by age group (contact-based).

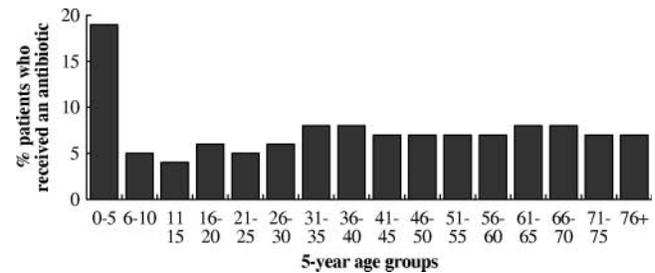


Figure 2. Percentage of patients who received an antibiotic for respiratory tract infections, by age group (population-based).

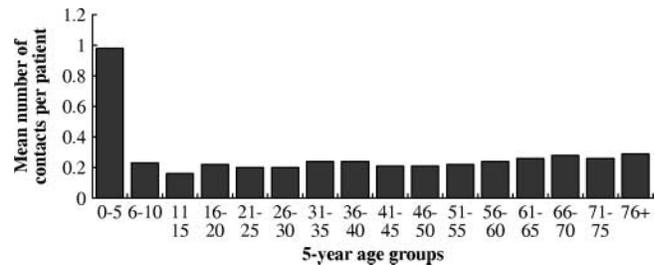


Figure 3. Mean number of respiratory tract infection contacts per patient, by age group.

received an antibiotic in about 25% of RTI contacts. The highest antibiotic prescribing rates (in almost 35% of RTI contacts) were seen for patients aged 31–65 years. Relating the number of patients receiving at least one antibiotic prescription for an RTI in the year 2000 to the total patients per age group in that year, children of age 0–5 years received by far the most (Figure 2, population-based). Figure 3 shows that these children also have the highest contact rate for RTIs.

In contacts with a respiratory diagnosis, 46% resulted in an antibiotic prescription, compared with 13% in contacts with respiratory symptoms only (Table 3). There was considerable variation in contact-based antibiotic prescribing rates between the clinical entities. High prescribing rates were seen in patients with sinusitis-like complaints (67%) or pneumonia (78%), whereas low rates were found for patients with upper RTIs (16%) (Table 3).

There was no difference in contact-based antibiotic prescribing between male and female patients, nor between patients with different types of insurance (Table 3), nor between different types of contact.

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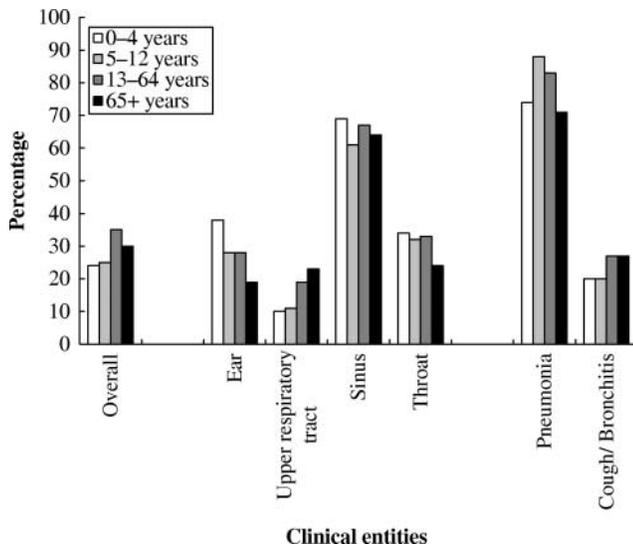


Figure 4. Antibiotic prescribing for respiratory tract clinical entities in four age groups (contact-based).

Figure 4 shows the contact-based antibiotic prescribing rates in four age groups for different clinical entities of RTI. Overall, children (0–12 years) received antibiotics less often (25% of contacts) than adolescents and adults (over 13 years) (34% of all contacts) ($\chi^2 = 506$, $df = 1$, $P < 0.001$). This trend was also seen for upper RTIs ($\chi^2 = 175$, $df = 1$, $P < 0.001$) and cough/bronchitis ($\chi^2 = 129$, $df = 1$, $P < 0.001$). On the other hand, children of age 0–4 years with ear complaints received more antibiotics (38%) than older patients with ear complaints (27%) ($\chi^2 = 86$, $df = 1$, $P < 0.001$). In throat complaints the elderly (over 65 years) received less antibiotics than younger patients ($\chi^2 = 24$, $df = 1$, $P < 0.001$). In cases of sinusitis-like complaints and pneumonia, age made no significant difference for antibiotic prescribing.

Discussion

In one-third of all contacts concerning RTIs, antibiotics were prescribed, with a considerable variation between different age groups and clinical entities. Surprisingly, for children (0–15 years) and the elderly (over 75 years), the lowest contact-based antibiotic prescribing rates for RTIs were found. Population-based, children of age 0–5 years received by far the most antibiotics for RTIs, probably due to a high frequency of RTI contacts in this age group. The highest contact-based antibiotic prescribing rates for RTIs were observed between the ages of 31 and 65. There was considerable variation in contact-based antibiotic prescribing rates between different age groups and clinical entities.

The validity of the results depends on the completeness and quality of the data used. Prescription records in the IPCI database can be assumed to be complete since participating GPs are not allowed to write paper prescriptions. Therefore, prescription rates of antibiotics in this study can be considered complete. In addition, GPs who keep patient records on a computer do not differ much from GPs with patient records on paper.¹⁰

ICPC codes and free text words were used to select contacts concerning RTIs. GPs who provide data to the IPCI database, are requested to use ICPC codes. However, for this analysis,

39% of the RTI contacts did not have an ICPC code, which emphasizes the importance of searching free text words in identifying RTI contacts. By excluding irrelevant contacts we attempted to minimize the number of false-positive contacts, but a certain amount of misclassification cannot be avoided. We were unable to differentiate between multiple visits pertaining to the same RTI episode, which may have caused an underestimation of the antibiotic prescribing rate. From a recent study, we know that 95% of all upper RTI episodes presented to general practice consist of only one contact with the GP. In lower RTIs, it would be somewhat lower, around 90%. So, the underestimation will not be more than 10%.

Population-based, children (0–5 years) received by far the most antibiotics for RTIs, but per contact, children were less likely to receive antibiotics, just like the elderly (over 75 years). Children and the elderly visit the GP more often than adults, probably because of more frequent (children) or more severe (elderly) RTI morbidity, but RTI visits less often result in antibiotic prescriptions. Low contact-based antibiotic prescribing rates for children with RTIs,¹¹ and a low antibiotic prescribing rate for the elderly (over 64 years)¹² were also found in the USA. Some studies found no association between antibiotic prescribing rates and patient age in cases of RTIs, but these studies excluded children.^{13,14}

We did not find a high population-based antibiotic prescription for the elderly (over 65 years), whereas others did.^{4,5} Probably this is because our population only comprised patients in general practice and not patients in institutes, such as homes for the aged, where antibiotics are often prescribed.¹⁵

The high contact-based antibiotic prescribing rate for RTIs in adults (31–65 years) could be explained by the fact that these are mainly working people. Perhaps these patients ask for an antibiotic more often or the GP feels the patient's pressure to prescribe an antibiotic.

In general, Dutch prescribing rates of antibiotics are relatively low compared to other European Union countries,¹⁶ the USA¹⁷ and Canada.¹⁸

The mean prescription rates for children with RTIs in this study are rather similar to those found in Dutch studies 10 years ago.¹⁹ In Germany, antibiotic prescribing rates for children with RTIs are similar,²⁰ but in the USA⁶ and Canada²¹ they are nearly twice as high.

There was a considerable variation in antibiotic prescribing rates between the different clinical entities. This relation between antibiotic prescribing rates and diagnoses has been found before.^{14,17,22} The varying role of bacterial and viral infections between clinical entities may be an explanation. The vast majority of upper RTIs have a viral aetiology,²³ whereas for lower RTIs this is about 60%.²⁴

We compared the contact-based antibiotic prescribing rates of Figure 4 with estimates of evidence-based antibiotic prescribing rates for RTIs that de Melker made several years ago²⁵ [based on the guidelines of the Dutch College of General Practice (Table 4)]. This revealed that antibiotics were over-prescribed in cases of upper RTIs, because for these clinical entities no antibiotics are indicated. For ear complaints the indications for antibiotics are more stringent for older than for younger children. Overall, appropriate prescription rates for otitis media should be around 15%. In line with current guidelines we saw that antibiotic prescribing rates in children with otitis media decreased with age. The indications for antibiotic treatment in tonsillitis

Table 4. Guidelines of the Dutch College of General Practitioners

Clinical entities—infections	Indications for antibiotic treatment
Upper respiratory tract	
Ear—acute otitis media	age 0–6 months: always age 7–24 months: in cases of relapse age >25 months: severe illness, worsening compared with previous contact, ear, nose or throat malformations
Upper respiratory tract infection	antibiotics not indicated
Sinus—sinusitis	more than 5 days complaints
Throat—tonsillitis	presence of peritonsillar infiltration presence of rheumatic fever severe illness
Lower respiratory tract	
Pneumonia	antibiotics always indicated
Cough/bronchitis	age 0–6 months: presence of fever age above 75 years: presence of fever other ages: presence of relevant comorbidity (heart failure)

are rather stringent and the relatively low prescribing rates are therefore plausible, close to de Melker's estimate of 30–40%. The finding that the elderly (over 65 years) with throat complaints received less antibiotics than younger patients (contact-based) is not supported by the literature. In cases of sinusitis-like complaints or pneumonia, contact-based antibiotic prescribing was not related to age. This may be because of the weight GPs give to these complaints, irrespective of patient age. In cases of sinusitis, the antibiotic prescribing rates are high compared to the estimation of de Melker that only 10% of antibiotics prescribed for sinusitis would be appropriate. For pneumonia, the antibiotic prescribing rates appeared to be low, because antibiotics are always indicated for this diagnosis. These relatively low antibiotic prescribing rates are most likely a consequence of including pneumonia-related follow-up visits. In cases of cough/bronchitis the antibiotic prescribing rates are not supported by the guidelines. This can be explained by the fact that the guideline about cough/bronchitis was not published at the time the consultations in the IPCI database were registered. Based on these data, it is difficult to state whether antibiotics are under- or over-prescribed, because we do not know the clinical factors of the patients (e.g. severity of illness, fever, duration of complaints). Recently, we finished a project about clinical determinants of under- and over-treatment of antibiotics for RTIs in general practice. Data will be published in the near future.

In conclusion, potential over-prescribing of antibiotics for RTIs occurs in the age group 31–65 years and in patients with upper RTIs, sinusitis and most likely acute bronchitis (contact-based). The management of these subgroups of patients should be addressed in quality assurance programmes. In developing these programmes, more information is needed on the reasons for inappropriate antibiotic use in certain groups of patients.

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References

1. Sampers, G. H. M. A. & Sturm, A. W. (1990). Antimicrobiële middelen in de eerste lijn bij luchtweginfecties. *Huisarts en Wetenschap* **33**, 220–2.
2. Wenzel, R. P. & Edmond, M. B. (2000). Managing antibiotic resistance. *New England Journal of Medicine* **343**, 1961–3.
3. Menown, I. B., Archbold, J. A., Bamford, K. B. *et al.* (1997). Community-acquired lower respiratory tract infection: implementation of an antibiotic protocol. *British Journal of Clinical Practice* **51**, 74–7.
4. Geneesmiddelen Informatie Project (GIP) (Dutch Drug Information Project) (2000). Volume en kosten per ATC-hoofdgroep naar leeftijd en geslacht (tabel 5a&b). In *GIPeilingen 1998, Kengetallen farmaceutische hulp*, pp. 30–3, (College voor Zorgverzekeringen (Health Care Insurance Board)), Amstelveen, the Netherlands.
5. Majeed, A. & Moser, K. (1999). Age- and sex-specific antibiotic prescribing patterns in general practice in England and Wales in 1996. *British Journal of General Practice* **49**, 735–6.
6. Nyquist, A. C., Gonzales, R., Steiner, J. F. *et al.* (1998). Antibiotic prescribing for children with colds, upper respiratory tract infections, and bronchitis. *Journal of the American Medical Association* **279**, 875–7.
7. Anonymous (1998). *ICPC-2: International Classification of Primary Care*. World Organization of National Colleges, Academies, and Academic Associations of General Practitioners/Family Physicians, Oxford, UK.
8. WHO Collaborating Centre for Drug Statistics Methodology (2004). Anatomical Therapeutic Chemical classification [Online.] <http://www.whocc.no/atcddd> (16 June 2004, date last accessed).
9. Vlug, A. E., van der Lei, J., Mosseveld, B. M. *et al.* (1999). Postmarketing surveillance based on electronic patient records of the IPCI project. *Methods of Informatics in Medicine* **38**, 339–44.
10. Westert, G. P., Hoonhout, L. H. F., de Bakker, D. H. *et al.* (2002). Huisartsen met en zonder elektronisch medisch dossier: weinig verschil in medisch handelen. *Huisarts en Wetenschap* **45**, 58–62.
11. Stone, S., Gonzales, R., Maselli, J. *et al.* (2000). Antibiotic prescribing for patients with colds, upper respiratory tract infections, and bronchitis: a national study of hospital-based emergency departments. *Annals of Emergency Medicine* **36**, 320–7.
12. Cantrell, R., Young, A. F. & Martin, B. C. (2002). Antibiotic prescribing in ambulatory care settings for adults with colds, upper respiratory tract infections, and bronchitis. *Clinical Therapeutics* **24**, 170–82.
13. Gonzales, R., Steiner, J. F. & Sande, M. A. (1997). Antibiotic prescribing for adults with colds, upper respiratory tract infections, and bronchitis by ambulatory care physicians. *Journal of the American Medical Association* **278**, 901–4.
14. Kuyvenhoven, M. M., Verheij, T. J. M., de Melker, R. *et al.* (2000). Antimicrobial agents in lower respiratory tract infections in Dutch general practice. *British Journal of General Practice* **50**, 133–4.
15. Meydani, S. N., Leka, L. S., Fine, B. C. *et al.* (2004). Vitamin E and respiratory tract infections in elderly nursing home residents: a randomised controlled trial. *Journal of the American Medical Association* **292**, 828–36.
16. Cars, O., Mölsted, S. & Melander, A. (2001). Variation in antibiotic use in the European Union. *Lancet* **357**, 1851–3.

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17. Steinman, M. A., Gonzales, R., Linder, J. A. *et al.* (2003). Changing use of antibiotics in community-based outpatient practice, 1991–1999. *Annals of Internal Medicine* **138**, 525–33.
18. Hutchinson, J. M., Jelinski, S., Hefferton, D. *et al.* (2001). Role of diagnostic labeling in antibiotic prescription. *Canadian Family Physician* **47**, 1217–24.
19. van der Ven-Daane, I., van der Ven, M., Buijnzeels, M. A. *et al.* (1992). Het voorschrijven van antibiotica aan kinderen in de huisartspraktijk. *Huisarts en Wetenschap* **35**, 272–4.
20. Schindler, C., Krappweis, J., Morgenstern, I. *et al.* (2003). Prescriptions of systemic antibiotics for children in Germany between 0 and 6 years. *Pharmacoepidemiology and Drug Safety* **12**, 113–20.
21. Wang, E. E., Einarson, T. R., Kellner, J. D. *et al.* (1999). Antibiotic prescribing for Canadian preschool children: evidence of overprescribing for viral respiratory infections. *Clinical Infectious Diseases* **29**, 155–60.
22. Akkerman, A. E., Kuyvenhoven, M. M., van der Wouden, J. C. *et al.* Prescribing antibiotics for respiratory tract infections by general practitioners: management and prescriber characteristics. *In press*.
23. Snow, V., Mottur-Pilson, C. & Gonzales, R. (2001). Principles of appropriate antibiotic use for treatment of nonspecific upper respiratory tract infections in adults. *Annals of Internal Medicine* **134**, 487–9.
24. Graffelman, A. W., Knuistingh Neven, A., le Cessie, S. *et al.* (2004). Pathogens involved in lower respiratory tract infections in general practice. *British Journal of General Practice* **54**, 15–19.
25. De Melker, R. A. (1998). Effectiviteit van antibiotica bij veelvoorkomende luchtweginfecties in de huisartspraktijk. *Nederlands Tijdschrift voor Geneeskunde* **142**, 452–6.