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Variation in formulary adherence in general practice over time (2003–2007)

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ABSTRACT

Objective. To study trends and variation in adherence to the main national formulary for the 20 most prevalent health problems in Dutch general practice over a 5-year period (2003–07).

Methods. Routine electronic medical records from a pool of 115 representative general practices were linked to the main national formulary. Analyses included over 2 million prescriptions for 246 391 patients. The outcome variable was whether or not the prescribed medication was congruent with recommendations in the national formulary. Trends and variation were analysed using three-level multilevel logistic regression analyses (general practice, patient, and prescription).

Results. The percentage of formulary adherent prescriptions for the 20 most prevalent health problems was 73–76% between 2003 and 2007. The percentage varied considerably between guidelines. Lowest adherence rates were found for acute bronchitis and acute upper respiratory infection. Interpractice variation was constant over time.

Conclusions. General practice information networks are useful for monitoring general patterns of formulary on a year-to-year basis. Formulary adherence is stable over time but varies across diagnoses, patients and general practices. In the past decade, efforts have been made to increase the level of formulary adherent prescribing. These general efforts managed to stabilize (variation in) adherence in a field where many other initiatives (e.g. by pharmaceutical companies) are undertaken to influence prescribing behaviour.

INTRODUCTION

The increasing number of drugs that have become available in recent decades has made prescribing increasingly complex, especially for GPs, who prescribe a large variety of drugs.[1] Evidence-based recommendations can support GPs in the prescribing process by reducing uncertainty about what drugs to choose for a specific health problem.[2] In the Netherlands, >80 guidelines were published by the Netherlands College of General Practitioners (NHG) since the late 1980s. The prescription recommendations in these guidelines are available in the NHG formulary. From 2002 onwards, the formulary was extended by recommendations that provide evidence-based advice for minor ailments for which no NHG guidelines are available.

Formularies such as the NHG formulary are supposed to reduce unwanted variation in medical practice.[3] Some studies indicate that formularies may decrease or stabilize variation in a market where more drugs are becoming available.[4,5] Variation in adherence to formularies can exist at different levels. Firstly, previous studies have shown that considerable variation exists between GPs in prescribing behaviour and adherence to evidence-based recommendations.[4–12] Secondly, adherence to formularies varies across patients. For some patient groups, physicians more often deviate from the formulary.[4–6,13–15] Thirdly, there are differences between health problems in level of formulary adherence.[4,9,10,15,16] A variety of reasons may explain these differences, such as the complexity of the health problem, the way the formulary for this particular health problem was developed, content of the recommendations, the publishing party and the amount of work the advice generates for the GP.[17,18] Finally, variation may change over time. Up to now, most studies have focused on adherence to formularies for a limited period of time, which is the reason why long-term developments are unknown. Furthermore, little research has been conducted on long-term developments in adherence variation. An exception is a study by De Jong et al., comparing variation in formulary adherence in the late 1980s to the situation in 2001, during which period many new guidelines had been introduced. The authors concluded that interpractice variation did not diminish between these dates; however, indications were found that guidelines tempered an increase in variation.[2] While many new guidelines became available during the last decades of the previous century, nowadays, the use of formularies is incorporated in daily clinical practice. Although the value of evidence-based practice is widely acknowledged, developments in formulary adherence are hardly monitored on a year-to-year basis. This study examines trends in adherence to the NHG formulary for a 5-year period: 2003–07. In addition, variation in formulary adherence at GP and patient level is studied for various health problems and for the different years.

METHODS

Study setting

Data were obtained by linking routine registration data collected in general practice between 2003 and 2007 to the database of the electronic version of the NHG formulary. General practice data were derived from the electronic medical records-based Netherlands Information Network of General Practice (LINH), a large and dynamic pool of general practices across the country that includes ~3% of all general practices in the Netherlands and >300 000 patients. The general practices are spread across the country and located in both rural and urbanized areas. Patients are representative for the whole population with respect to age, gender, consultation behaviour and type of medication used.[19] GPs are representative as well. Comparisons based upon claim and pharmacy data showed that there were only small differences in medical practice between GPs participating in LINH and non-participating GPs.[19] GPs prescribe ~75% to 80% of all medication in the Netherlands.[20,21]

LINH GPs register every prescription. These are coded using the Anatomical Therapeutical Chemical (ATC) coding system.[20] They use the International Classification for Primary Care (ICPC) to identify the reason to prescribe.[22] LINH studies are conducted in keeping with Dutch legislation on privacy, which stipulates that obtaining informed consent is not obligatory for observational studies.

The electronic version of the NHG formulary stores formulary recommendations. An important element is a list of all ‘diagnosis–drug combinations’ (DDCs) containing all combinations of ICPC codes with recommended drugs (ATC codes). We had access to the 2006 DDC list. Linkage of the LINH database to the DDC list was based on the four-digit ICPC code and the full ATC code. Our analyses were limited to the top 20 most prevalent health problems encountered in general practice.[23] For these health conditions, no major innovative drugs were introduced during the study period.

Only patients with at least one of the selected health problems were included. In this period, the overall number of prescriptions per year in the database ranged from 1.6 to 2.2 million (Table 1). Seventy per cent of all prescriptions were ICPC coded. Practices were excluded if they had overall <3000 prescriptions for the top 20 diagnoses. This ensured the exclusion of practices that had low levels of ICPC coding.

[TABLE 1]

MEASUREMENTS

Outcome.

Prescriptions for the 20 most prevalent health problems (ICPC) were selected. For each prescription, it was checked whether the prescribed drug was listed in the NHG formulary for this particular ICPC and a dichotomous variable was created (congruent/not congruent). The ATC-4 level was used to determine whether or not a prescription was formulary adherent: not only the specific drug listed in the formulary was considered adherent but also drugs with the same mechanism. An example: when prescribing for sleep problems, the formulary recommends oxazepam (N05BA04). In our study, not only oxazepam is considered adherent but also all other drugs with ATC code N05BA. The reason is that in some NHG guidelines, specific drugs are mentioned as just an example for a group as a whole.

Other variables.

For each prescription, we created dichotomous variables for the 20 health problem to indicate whether or not the prescription was written for this particular health problem. In addition, we created variables for the year in which the prescription was written.

Control variables included at the patient level were year of birth and gender. In addition, the total number of prescriptions for a top 20 health problem per year, per diagnosis and for the overall period were calculated as well as the total number of top 20 health problems per year, per diagnosis and for the overall period.

Since the registration habits of GPs are associated with the type of general practice information system (GPIS) they use, this variable was included in all analyses as a control variable. GPIS is used in general practices to register patient contacts, prescriptions, administrative matters, etc. Participating general practices used six different systems. Practice characteristics such as type of practice and being a dispensing practice were not associated with formulary adherence and therefore not used as control variables.

Analyses

Firstly, we calculated the ‘proportion of formulary adherent prescriptions per ICPC per year’ taking into account clustering at the general practice level. Secondly, a three-level multilevel logistic regression analysis was used to analyse ‘variation in formulary adherence at the practice and patient level’ for each ICPC over the whole 5-year period. Multilevel logistic regression analyses were used to take the nested structure of the data into account.[24] For each particular health problem, we estimated three models: (i) the empty model, (ii) adding year of prescription and (iii) adding patient characteristics. Median odds ratios (MORs) were calculated to interpret variance at the practice and patient level. The MOR translates the variance estimated in the multilevel model into an odds ratio scale.[5,25] If the MOR at the practice level equals one, then this means general practices do not differ at all in formulary adherence. If the MOR is high, then the variation in formulary adherence between practices is substantial.[5] Finally, three-level multilevel logistic analyses were performed to study the stability of the variation for all 20 health problems together over time. For each year, we estimated two models: (i) empty model and (ii) adding the ICPC codes. MLWin 2.11 and Stata 10.0 were used to analyse the data.[26]

RESULTS

In total, 2 436 729 prescriptions written to 246 391 patients in 115 general practices from 2003 to 2007 were included (Table 2); individual patients received on average 9.9 prescriptions for the 20 most prevalent health problems (SD = 18.3). Most prescriptions were written for hypertension without complications (22% of the prescriptions for the 20 most prevalent health problems), followed by diabetes mellitus (11.6%) and asthma (5.8%) (Table 3). The number of patients was highest for dermatitis (contact/allergic), hypertension without complications and dermatophytosis, respectively. The number of prescribed drugs (DU-90, the number of different drugs that cover 90% of all drugs prescribed for this health problem in a single year) varies from 4 to 19 between health problems.

[TABLE 2]

Proportion of formulary adherent prescriptions

Overall, percentages of formulary adherence for the 20 most prevalent diagnoses ranged from 74% in 2007 to 76% in 2003 and 2004 (75% in 2005 and 2006). For four diagnoses, the proportion of formulary adherent prescriptions exceeded 90% in at least 4 years. These were constipation, sleeping disorders, lipid disorders and cystitis/urinary infection other. For these health problems, DU-90 is lower than for other health conditions, so GPs have a lower range of drugs they prescribe for these diagnoses. Two respiratory diagnoses had less than half of the prescriptions according to formulary recommendations: acute upper respiratory infection and acute bronchitis (Table 4). For acute upper respiratory infection, GPs prescribed many different drugs. In 2007, 14% of all prescriptions for acute upper respiratory infection included doxycycline, a recommended drug. The two most frequently prescribed non-recommended drugs for acute upper respiratory infection were codeine (R05DA04, 11%) and salbutamol (R03AC02, 5%). In the case of acute bronchitis, about half of the prescriptions were for non-recommended antibiotics.

[TABLE 3,4]

The level of formulary adherence is not related to the number of drug classes (ATC-4) recommended in the NHG formulary. To illustrate this, there are two health problems for which only one drug class is recommended respectively: lipid disorders and acute bronchitis. While for lipid disorders the level of formulary adherence is >90% in all years, acute bronchitis has the lowest level of formulary adherence.

For seven health problems, the proportion of adherent prescriptions was >5% lower in 2007: ischemic heart disease without angina, depression, COPD, asthma, dermatophytosis, dermatitis (contact/allergic) and diabetes mellitus.

Variation at practice and patient level per diagnosis

In the next step, we estimated variation at the practice and patient level for the 20 individual health problems (Table 5). While the level of adherence varies considerably between diagnoses (Table 4), this is less true for the variation at the practice level: MORs range from 1.5 to 1.7 for 14 of the 20 health problems. Variation at the practice level is highest for acute bronchitis (MOR = 2.3), followed by sleeping disorders (MOR = 1.9). Interpractice variation is lowest for oral contraception (MOR = 1.1), followed by COPD, allergic rhinitis and ischemic heart disease (MOR = 1.4). Differences in variation are larger at the patient level. Most variation is found for lipid disorders (MOR between 7.6 and 7.8) and sleeping disorders (MOR between 7.0 and 7.6). Health problems with less variation at the patient level are oral contraception (MOR 1.4–1.5) and upper respiratory infection (MOR 1.7–1.9).

[TABLE 5]

Variation in overall formulary adherence >5 years

Table 6 shows the variation in overall formulary adherence for the 20 included health problems over the course of 5 years. The interpractice variation is constant over time: MORs are 1.3 for all years (Table 5). Likewise, variation at the patient level is almost constant over time, although MORs show a slight drop from 3.3 in 2003 to 2.9 in 2007.

[TABLE 6]

DISCUSSION

Main results and comparison with existing literature

Formulary adherence in Dutch general practice was monitored for the years 2003–07. Adherence was defined as the choice of a drug that was recommended in the NHG formulary for 1 of the 20 most prevalent health problems in general practice. On average, the level of adherence for these 20 health problems was 73–76%, which is in the range of previous studies on adherence to guidelines.[10,15,16] Formulary adherence was rather stable over time, although for a minority of the 20 health problems, a decrease was observed. Differences in formulary adherence between health problems were considerable, ranging from 3% for acute bronchitis followed by 40% for upper respiratory infection to >90% for four other diagnoses. Such

differences were found in earlier studies as well.[4,9,10,15,16] GPs chose mainly the same drugs for the latter category (DU-90). The low formulary adherence for acute bronchitis can for a large part be attributed to the prescribing of non-recommended antibiotics. Apparently, even in the Netherlands where antibiotic prescribing is low compared to other Western countries,[27] antibiotics are prescribed for diagnoses for which they are not indicated.

GPs look at individual patients when prescribing. A meta-analysis on reasons why physicians did not follow guidelines showed that doctors' main argument was their concern for the individual patient coupled with scepticism about applying general research findings to individuals.[28] We did indeed find that variation at the patient level is clearly higher than at the practice level, albeit slightly decreasing. This shows that GPs make individual considerations for each patient. Implementation of guidelines is therefore a complex process and review studies state that a combination of strategies to improve the implementation of guidelines is usually most effective.[17,29–32] Over the past 5–10 years, considerable efforts have been made to improve formulary adherence such as via professionalization in peer group reviewing and developing prescription indicators for benchmark purposes.[4,33,34]

An important intervention was the introduction of the electronic decision support system (DSS) at the national level in 1999. Until 2002, considerable efforts were made to implement DSS in general practice. One element of this implementation program was that savings made in prescribing at the national level were returned to GPs by increasing the budget for additional staff. Between 1999 and 2002, the use of DSS steadily increased. GPs who used DSS in 2001 were more adherent to the guidelines.[2] Increasing DSS use may thus further increase formulary adherence. However, the implementation program ceased in 2002 and was followed by a stagnation in DSS use between 2002 and 2006.[23] It may well be that, with the current non-compulsory use of DSS, the maximum effect on formulary adherence has been reached.

Strengths and limitations of the study

Data came from a large nationwide general practice network. Information is registered in an electronic information system—usually during patient contacts. A large majority of the general practices in the Netherlands have a computerized patient registration system. The GPs in our study did not differ from other GPs in this respect. In addition, previous research showed that there were only small differences in medical practice between GPs participating in the LINH network and other GPs, except that LINH GPs prescribed antibiotics slightly less often.[35,36]

To measure adherence, a so-called DDCs approach was used: did the formulary recommend the prescribed drug for a specific diagnosis?[16,23] An advantage of this approach is that it quickly provides an overview of whether GPs prescribed recommended medication for a whole range of health problems, which is why it is useful for signalling potential general problem areas for policy making.[10] The availability of indications in itself is an advantage of this approach. Several studies on adherence to recommendations only include information on prescribed drugs. Such an approach usually involves working with nationwide pharmacy or reimbursement claim data. However, formularies usually refer to a particular health problem. Many drugs, such as NSAIDs, betablockers and antidepressants, are prescribed for different health conditions and interpretation problems may arise if no information on the diagnosis is included.[37–39]

The DDC approach also has limitations. Guidelines are usually more complicated than just recommending a certain type of drug. Sometimes, there are age restrictions or recommendations against prescribing a drug in case of contra-indications or co-morbidities. We accounted for co-morbidity by including the total number of prescriptions and the total number of diagnoses in the analyses. Another neglected element in the DDC approach is restrictive prescribing. A study on antibiotics showed that adherence to recommendations on type of medication was not strongly correlated to following recommendations on such restrictive prescribing[10,40], an element that is not taken into account in the DDC approach. The so-called progressive schemes (recommending to prescribe first drug A, and if it is not effective, to follow on with drug B) included in some guidelines were also not taken into account: all drugs recommended in the guidelines were considered adherent. To address these specific problems, more detailed indicators are necessary.[10,41] Working with such indicators yields more detailed information on quality of care than the other approaches but is time consuming and often requires considerable efforts to extract data from computer systems.

We looked exclusively at adherence to the NHG formulary, while other formularies also exist in the Netherlands. These formularies are usually regionally based. Since the participating practices were widely distributed across the country and recommendations in other formularies are often based on those from the NHG formulary, it is plausible to assume that our results reflect the Dutch situation. In our study, the 2006

list of DDCs was used. For a number of the included health problems, NHG guidelines changed between 2003 and 2007. Our results, however, showed that this did not affect GPs' choices in type of medication. There may be several reasons for this. Sometimes GPs are 'ahead of the guidelines'. This was, for example, the case for the depression guideline. GPs widely prescribed SSRIs, before they were recommended in the guidelines. On the other hand, prescription behaviour is hard to change and it may take some more time before GPs take over advises in the clinical guidelines.[2] Also, guidelines sometimes only change recommendations at the ATC-5 level while we looked at the ATC-4 level, at this lower level changes may take place.

Another concern is the role of prescriptions initiated by a specialist that are subsequently followed by repeat prescriptions from GPs since these may influence both the level of adherence and the variation in adherence between general practices. If a GP refers relatively more often to a medical specialist, he or she may also prescribe more repeat prescriptions initiated by specialists that more often deviate from GP guidelines.[1] We were not able to investigate this influence, which is a limitation of this study. Moreover, we could not distinguish between first and repeat prescriptions for all GPs. Therefore, we included all prescriptions, which may also have an impact on our results. It may well be that GPs who adhere strictly to the guidelines are also less likely to issue repeat prescriptions (for example in the case of benzodiazepines).

CONCLUSIONS

General practice routine registration data are a good source of information for monitoring formulary adherence on an annual basis. Our results show that formulary adherence is relatively stable over time but varies across diagnoses, patients and GPs. In the last two decades, several efforts have been made to increase the level of formulary adherent prescribing in the Netherlands. These general efforts managed to stabilize the level of adherence in a field where many other initiatives are undertaken to influence prescribing behaviour (e.g. by pharmaceutical companies). To increase the level of adherence, a more intensive approach seems necessary.

REFERENCES

1 de Bakker DH, Coffie DS, Heerdink ER, van Dijk L, Groenewegen PP.Determinants of the range of drugs prescribed in general practice: a cross-sectional analysis. BMC Health Serv Res 2007; 7: 132.
2 de Jong JD, Groenewegen PP, Spreeuwenberg P, Schellevis F, Westert GP. Do guidelines create uniformity in medical practice? Soc Sci Med 2010; 70: 209–16.
3 Grilli R, Magrini N, Penna A, Mura G, Liberati A. Practice guidelines developed by specialty societies: the need for a critical appraisal.
Lancet 2000; 355: 103–6.
4 de Jong JD, Groenewegen PP, Spreeuwenberg P, Westert GP, de Bakker DH. Do decision support systems influence variation in prescription? BMC Health Serv Res 2009; 9: 20.
5 Ohlsson H, Lindblad U, Lithman T et al. Understanding adherence to official guidelines on statin prescribing in primary health care—a multi-level methodological approach. Eur J Clin Pharmacol 2005; 61: 657–65.
6 Davis PB, Yee RL, Millar J. Accounting for medical variation: the case of prescribing activity in a New Zealand general practice sample. Soc Sci Med 1994; 39: 367–74.
7 Hakansson A, Andersson H, Cars H, Melander A. Prescribing, prescription costs and adherence to formulary committee recommendations: long-term differences between physicians in public and private care. Eur J Clin Pharmacol 2001; 57: 65–70.
8 Ohlsson H, Merlo J. Understanding the effects of a decentralized budget on physicians' compliance with guidelines for statin prescription— a multilevel methodological approach. BMC Health Serv Res 2007; 7: 68.
9 Ohlsson H, Merlo J. Is physician adherence to prescription guidelines a general trait of health care practices or dependent on drug type? A multilevel logistic regression analysis in South Sweden. Pharmacoepidemiol Drug Saf 2009; 18: 682–90.
10 van Roosmalen MS, Braspenning JC, De Smet PA, Grol RP. Antibiotic prescribing in primary care: first choice and restrictive prescribing are two different traits. Qual Saf Health Care 2007; 16: 105–9.
11 Martens JD, van der WT, Severens JL et al. The effect of computer reminders on GPs' prescribing behaviour: a cluster-randomised trial. Int J Med Inform 2007; 76 (suppl 3)): S403–16.

12 Ong DS, Kuyvenhoven MM, van Dijk L, Verheij TJ. Antibiotics for respiratory, ear and urinary tract disorders and consistency among GPs. J Antimicrob Chemother 2008; 62: 587–92.
13 Stewart RE, Vroegop S, Kamps GB, van der Werf GT, Meyboomde Jong B. Factors influencing adherence to guidelines in general practice. Int J Technol Assess Health Care 2003; 19: 546–54.
14 Kasje WN, Denig P, Stewart RE, de Graeff PA, Haaijer-Ruskamp FM. Physician, organisational and patient characteristics explaining the use of angiotensin converting enzyme inhibitors in heart failure treatment: a multilevel study. Eur J Clin Pharmacol 2005; 61: 145–51.
15 Kamps G, Stewart R, van Der WG, Schuling J, Jong BM. Adherence to the guidelines of a regional formulary. Fam Pract 2000; 17: 254–60.
16 Groenhof F, Wefers Bettink C, van Dijk L, Van der Veen WJ, Meijboom-de Jong B. Adherence to pharmacotherapeutic advice in the guidelines of the Dutch College of General Practitioners.
In: Westert GP, Jabaaij L, Schuling J (ed).Morbidty, Performance and Quality in Primary Care. Dutch General Practice on Stage. Oxon, UK: Radcliffe publishing, 2006, pp.
219–25.
17 Grol R, Grimshaw J. From best evidence to best practice: effective implementation of change in patients' care. Lancet 2003; 362: 1225–30.
18 van den Berg MJ, de Bakker DH, Spreeuwenberg P et al. Labour intensity of guidelines may have a greater effect on adherence than GPs' workload. BMC Fam Pract 2009; 10: 74.
19 Verheij RA, Van Dijk CE, Abrahamse H et al. Landelijk Informatienetwerk Huisartsenzorg. Feiten en cijfers over huisartsenzorg in Nederland. Utrecht, the Netherlands: 2008.
20 GIP. www.gipdatabank.nl. 2009 (accessed on 27 July 2010).
21 van Dijk L. Prescription in Dutch general practice. In: Westert GP, Jabaaij L, Schellevis FG (ed). Morbidity, Performance and Quality in Primary Care, Oxon, UK: Radcliffe Publishing Ltd, 2006, pp. 115–24.
22 Lamberts H, Wood M, Hofmans-Okkes I. The International Classification of Primary Care in the European Community, with a Multilanguage Layer. Oxford, UK: Oxford University Press, 1987.
23 Volkers AC, van Dijk L, Wolters I, de Bakker DH. Formularia in de huisartspraktijk. Utrecht, The Netherlands: NIVEL, 2008.
24 Snijders TAB, Bosker RJ. Multilevel Analysis. An Introduction to Basic Ans Advanced Multilevel Modeling. London: Sage Publications, 1999.
25 Larsen K,Merlo J. Appropriate assessment of neighborhood effects on individual health: integrating random and fixed effects in multilevel logistic regression. Am J Epidemiol 2005; 161: 81–8.
26 Rasbash J, Steele F, Browne WJ, Goldstein H. A User's Guide to MLwiN. Version 2.10. Bristol, UK: Center for Multilevel Modelling, 2009.
27 Cars O, Molstad S, Melander A. Variation in antibiotic use in the European Union. Lancet 2001; 357: 1851–3.
28 Carlsen B, Glenton C, Pope C. Thou shalt versus thou shalt not: a meta-synthesis of GPs' attitudes to clinical practice guidelines.
Br J Gen Pract 2007; 57: 971–8.
29 Wensing M, van der WT, Grol R. Implementing guidelines and innovations in general practice: which interventions are effective? Br J Gen Pract 1998; 48: 991–7.
30 Grimshaw JM, Thomas RE, MacLennan G et al. Effectiveness and efficiency of guideline dissemination and implementation strategies.
Health Technol Assess 2004; 8: iii-72.
31 Francke AL, Smit MC, de Veer AJ, Mistiaen P. Factors influencing the implementation of clinical guidelines for health care professionals: a systematic meta-review. BMC Med Inform Decis Mak 2008; 8: 38.
32 Grol R, Berwick DM, Wensing M. On the trail of quality and safety in health care. BMJ 2008; 336: 74–6.
33 Florentinus SR, van Hulten R, KramerM et al. Which pharmacists contribute to high-level pharmacotherapy audit meetings with general practitioners? Ann Pharmacother 2006; 40: 1640–6.
34 van Dijk L, de Bakker DH. Professionalization of Dutch PRGs and volume and costs of frequently prescribed drugs. Zeitschrift fu¨r Gesundheitswissenschaften 2002; 10: 292–304.
35 Akkerman AE, Kuyvenhoven MM, Verheij TJ, van Dijk L. Antibiotics in Dutch general practice: nationwide electronic GP database and national reimbursement rates. Pharmacoepidemiol Drug Saf 2008; 17: 378–83.
36 Westert GP, Hoonhout L, de Bakker DH, Van den Hoogen H, Schellevis FG. Huisartsen met en zonder elektronisch medisch dossier: weinig verschil in medisch handelen. [GPs with and without electronic medical records: little difference in their medical practice.]. Huisarts en Wetenschap 2002; 45: 58–62.
37 Van Wijk BLG. Adherence and Persistence with Antihypertensive Drugs. Utrecht, the Netherlands: Utrecht University, 2006.

38 Florentinus SR. New Drugs in General Practices: Prescribing Patterns and External influences. Utrecht, the Netherlands: Universiteit Utrecht, 2006.
39 Gardarsdottir H, Heerdink ER, van Dijk L, Egberts AC. Indications for antidepressant drug prescribing in general practice in the Netherlands. J Affect Disord 2007; 98: 109–15.
40 van Dijk L, Schiere AM, Braspenning J. Voorschrijven van antibiotica.
In: Braspenning J, Schellevis FG, Grol RPTM (ed).
Tweede Nationale Studie naar ziekten en verrichtingen in de huisartspraktijk. Kwaliteit huisartsenzorg belicht. [Second Dutch National Survey of General Practice. Spotlight on quality of GP care.], Nijmegen, The Netherlands:, 2004, pp. 103–115.
41 Martirosyan L, Braspenning J, Denig P et al. Prescribing quality indicators of type 2 diabetes mellitus ambulatory care. Qual Saf Health Care 2008; 17: 318–23.

TABLES

TABLE 1 *Practices, patients and prescriptions per year*

	2003	2004	2005	2006	2007
Number of practices	82	73	70	69	75
Number of patients with at least one top 20 ICPC[a]	112 183	100 004	94 431	89 924	100 910
Number of prescriptions top 20 ICPC	517 693	457 367	441 813	446 027	537 829

[a]Practices and patients can be included in >1 year. Total number of practices included = 115 and total number of patients = 246 391.

TABLE 2 *Characteristics of patients with at least one of the selected diagnoses in 2003–07 (n = 246 391)*

Women (%)	59.3
Year of birth (%)	
Before 1930	9.1
1930–39	9.8
1940–49	13.0
1950–59	14.5
1960–69	15.0
1970–79	13.1
1980–89	12.1
1990 and later	13.4
Number of prescriptions, mean (SD)	9.8 (18.3)
Number of diagnoses, mean (SD)	1.9 (1.3)

TABLE 3 *Number of prescriptions, patients, recommended drugs and prescribed drugs (DU-90) per ICPC*

ICPC	Health problem	Number of prescriptions, 2003–07	Patients[a] (n = 246 391), 2003–07	Number of recommended drugs classes in NHG formulary (ATC4)	DU-90%, 2008[b]
D12	Constipation	60 633	17 934	4	6
K74	Ischemic heart disease no angina	72 285	6930	5	15
K86	Hypertension uncomplicated	536 858	39 238	7	16
K87	Hypertension complicated	73 416	5681	7	16
L03	Low back symptom/complaint	53 808	20 446	13	11
P01	Feeling anxious/nervous/tense	69 913	12 005	5	7
P06	Sleep disturbance	134 861	19 652	3	5
P76	Depressive disorder	127 549	13 708	3	9
R05	Cough	82 228	38 795	2	18
R74	Upper respiratory infection acute	51 803	28 173	4	16
R78	Acute bronchitus/bronchiolitis	66 020	25 419	1	15
R95	COPD	82 873	8464	9	16
R96	Asthma	140 501	21 561	6	9
R97	Allergic rhinitis	108 616	26 268	4	6
S74	Dermatophytosis	76 257	38 808	6	14
S88	Dermatitis contact/allergic	105 500	42 888	9	19
T90	Diabetes non-insulin dependent	282 330	16 597	5	16
T93	Lipid disorder	111 877	15 089	1	4
U71	Cystitis/urinary infection other	85 772	35 943	7	9
W11	Contraception oral	113 679	37 106	2	2
	Top 20 overall	2 436 729	246 391		

[a]Patients can have >1 ICPC code, which is why the sum of the number of patients per diagnosis does not add up to 246 391.
[b]The number of different drugs (ATC-4) that cover 90% of all drugs prescribed for this ICPC code.

TABLE 4 *Formulary adherence in prescribing medication for the 20 most frequently registered diseases in general practice between 2003 and 2007: results from multilevel analyses per diagnosis*[a]

		% Formulary adherent (ATC4)				
ICPC	Health problem	2003	2004	2005	2006	2007
D12	Constipation	91	89	94	91	92
K74	Ischemic heart disease no angina	81	81	80	79	75
K86	Hypertension uncomplicated	81	81	81	81	78
K87	Hypertension complicated	73	76	74	72	75
L03	Low back symptom/complaint	83	81	79	84	83
P01	Feeling anxious/nervous/tense	87	88	89	88	87
P06	Sleep disturbance	94	93	91	92	90
P76	Depressive disorder	73	71	68	68	66
R05	Cough	53	57	60	58	54
R74	Upper respiratory infection acute	40	43	40	40	39
R78	Acute bronchitus/bronchiolitis	3	4	4	3	3
R95	COPD	76	70	69	70	66
R96	Asthma	68	66	63	61	58
R97	Allergic rhinitis	80	80	81	80	81
S74	Dermatophytosis	87	87	85	84	82
S88	Dermatitis contact/allergic	58	48	47	53	53
T90	Diabetes non-insulin dependent	71	70	65	64	63
T93	Lipid disorder	93	93	91	92	91
U71	Cystitis/urinary infection other	90	91	92	93	90
W11	Contraception oral	68	69	69	68	69
	Top 20 overall	76	76	75	75	73

[a]Two-levels: general practices and prescriptions; all analyses were controlled for GPIS (GP level).

TABLE 5 *Variation at patient and general practice level in formulary adherence in prescribing medication for the 20 most frequently registered diseases in general practice between 2003 and 2007*[a]

ICPC	Health problem	Practice (n = 115)		Patient (n = 246 391)[b]	
		Variance (se)	MORs (95% confidence intervals)	Variance (SE)	MORs (95% confidence intervals)
D12	Constipation	0.34 (0.05)	1.7 (1.6–1.9)	2.61 (0.07)	4.6 (4.5–4.8)
K74	Ischemic heart disease no angina	0.15 (0.03)	1.4 (1.4–1.5)	2.82 (0.06)	4.1 (3.9–4.2)
K86	Hypertension uncomplicated	0.24 (0.03)	1.6 (1.5–1.6)	1.95 (0.02)	3.8 (3.8–3.8)
K87	Hypertension complicated	0.17 (0.04)	1.5 (1.4–1.6)	1.69 (0.02)	3.4 (3.3–3.5)
L03	Low back symptom/complaint	0.23 (0.04)	1.6 (1.5–1.7)	1.37 (0.04)	3.0 (2.9–3.1)
P01	Feeling anxious/nervous/tense	0.23 (0.04)	1.6 (1.4–1.7)	3.03 (0.07)	5.2 (5.0–5.4)
P06	Sleep disturbance	0.44 (0.07)	1.9 (1.7–2.1)	4.58 (0.08)	7.6 (7.4–7.9)
P76	Depressive disorder	0.19 (0.03)	1.5 (1.4–1.6)	2.56 (0.04)	4.6 (4.5–4.7)
R05	Cough	0.26 (0.04)	1.6 (1.5–1.7)	1.14 (0.02)	2.8 (2.7–2.8)
R74	Upper respiratory infection acute	0.28 (0.04)	1.7 (1.5–1.8)	0.34 (0.04)	1.7 (1.7–1.8)
R78	Acute bronchitus/bronchiolitis	0.78 (0.13)	2.3 (2.0–2.6)	3.34 (0.14)	5.7 (5.3–6.1)
R95	COPD	0.12 (0.02)	1.4 (1.3–1.5)	1.52 (0.04)	3.2 (3.1–3.3)
R96	Asthma	0.30 (0.04)	1.7 (1.6–1.8)	1.44 (0.03)	3.1 (3.1–3.2)
R97	Allergic rhinitis	0.13 (0.02)	1.4 (1.3–1.5)	1.28 (0.03)	2.9 (2.9–3.0)
S74	Dermatophytosis	0.21 (0.03)	1.5 (1.4–1.6)	2.54 (0.06)	4.5 (4.4–4.7)
S88	Dermatitis contact/allergic	0.23 (0.03)	1.6 (1.5–1.7)	0.97 (0.02)	2.5 (2.5–2.6)
T90	Diabetes non-insulin dependent	0.23 (0.03)	1.5 (1.5–1.7)	1.29 (0.02)	2.9 (2.9–3.0)
T93	Lipid disorder	0.23 (0.04)	1.6 (1.4–1.7)	4.67 (0.08)	7.8 (7.5–8.1)
U71	Cystitis/urinary infection other	0.35 (0.05)	1.7 (1.6–1.9)	1.21 (0.04)	2.8 (2.8–2.9)
W11	Contraception oral	0.01 (0.00)	1.1 (1.1–1.1)	0.15 (0.00)	1.4 (1.4–1.5)

[a]Variables included in each analysis: GPIS, year, year of birth patient (centred), number of prescriptions for this ICPC patient (centred) and gender of patient.
[b]For number of patients per health problem, see Table 3.

TABLE 6 *Variation at patient and general practice level in overall formulary adherence (top 20 ICPCs) in prescribing medication per year* [a,b]

Year	Practice		Patient	
	Variance (SE)	MOR (95% CI)	Variance (SE)	MOR (95% CI)
2003	0.08 (0.05–010)	1.3 (1.2–1.3)	1.57 (1.54–1.60)	3.3 (3.3–3.3)
2004	0.07 (0.05–010)	1.3 (1.2–1.3)	1.51 (1.48–1.54)	3.2 (3.2–3.2)
2005	0.08 (0.05–0.11)	1.3 (1.2–1.4)	1.41 (1.38–1.44)	3.1 (3.1–3.1)
2006	0.07 (0.04–0.09)	1.3 (1.2–1.3)	1.36 (1.34–1.39)	3.0 (3.0–3.1)
2007	0.08 (0.05–0.10)	1.3 (1.2–1.4)	1.23 (1.20–1.25)	2.9 (2.8–2.9)

[a]All models included GPIS as a control variable.
[b]Models includes 19 dummies for diagnoses, P76 = reference.