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Agreement between self-reported and pharmacy data on medication use in the Northern Finland 1966 Birth Cohort

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Key words
agreement, pharmacy data, questionnaire, register, reliability, self-report

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Abstract

Objective: To compare self-reported (SR) medication use and pharmacy data for major psychoactive medications and three classes of medications used for different indications, and to determine the socio-economic factors associated with the congruence.

Methods: Postal questionnaire data collected in 1997 were compared with the register of the Social Insurance Institution of Finland on the reimbursed prescriptions purchased during 1997. Altogether 7625 subjects were included in this study. Drugs were categorized according to the Anatomical Therapeutic Chemical (ATC) system.

Results: Kappa values were 0.77, 0.68, 0.84, 0.92 and 0.55 for antipsychotics, antidepressants, antiepileptics, antidiabetics and beta-blocking agents, respectively. Prevalence-adjusted and bias-adjusted kappa values were almost perfect (0.98–1.00). Reliability of antipsychotics use was better for married subjects than for those who were not married; and of antidepressants use for highly educated and married subjects than for those who were less educated and were not married. Altogether 414 (5.4%) responders and 285 (7.1%) non-responders had used at least one of the selected medications.

Conclusion: Agreement between the SR and pharmacy data was moderate for psychoactive medication use. Even though data collected by postal questionnaire may underestimate the prevalence of medication use due to non-participation it can be assumed accurate enough for study purposes.

Introduction

Postal questionnaire is a reasonably simple way of collecting data from large samples, and a lot of population studies are hence based on questionnaire data. However, the reliability of data obtained with self-report inquiries relies on the ability and will of subjects to reply accurately (Boudreau *et al.*, 2004), as well as on data collection methods and the structure of the questionnaire (Klungel *et al.*, 2000). Monster *et al.* (2002) stated that pharmacy data constitute an easily obtainable and reliable tool in epidemiological studies. Pharmacy data are also unlikely to underestimate drug users (Curtis *et al.*, 2006).

The accuracy of self-reported medication use (SR data) has been shown to be reasonably good in many studies of selected populations (e.g. Kwon *et al.*, 2003; Boudreau *et al.*, 2004; Glintborg *et al.*, 2007). Guénette *et al.* (2005), however, concluding that self-reported measures of adherence exhibited poor agreement with those based on pharmacy records. We found a few population based studies (e.g. Haukka *et al.*, 2007; Nielsen *et al.*, 2008; Skurtveit *et al.*, 2008), who also studied the SR data on psychoactive medications.

Recall of medication use varies with the type of drug (e.g. Van den Brandt *et al.*, 1991). According to Caskie *et al.* (2006) medications used for serious conditions or on a regular basis are recalled well. Glintborg *et al.* (2007) found SR data reliable when estimating recent use of cardiovascular and antidiabetic drugs. Drugs used for disorders of the central nervous system have been shown to have lower degree of correct reporting than some other medications (van den Brandt *et al.*, 1991). When evaluating psychoactive medication use, people may be reluctant to report the use, or the psychological indication itself may lead to poor recall (van den Brandt *et al.*, 1991; Cotterchio *et al.*, 1999). However, the agreement between personal interview and register-based data has been shown to be good for most psychotropic drugs (Haukka *et al.*, 2007). Also Nielsen *et al.* (2008) found substantial agreement for antipsychotics and antidepressants. Boudreau *et al.* (2004) found only moderate agreement between SR and pharmacy data on antidepressant use, but Kwon *et al.* (2003) found better agreement than what they had expected.

Gender has not been shown to influence recall of drug consumption, whereas increasing age decreases the level of recall (van den Brandt *et al.*, 1991; West *et al.*, 1995). Having low household income, being not married and having poor health have been associated with poorer self-reporting (Cotterchio *et al.*, 1999; Caskie and Willis, 2004). Skurtveit *et al.* (2008) found better specificity for psychoactive medications compared to some other medications in a study of adolescents.

We compared the SR data and pharmacy data for major psychoactive medications (antipsychotics and antidepressants), and three classes of medications used for different indications (antiepileptics, antidiabetics and beta-blocking agents), in a large birth cohort. To study the methods of data collection is essential in order to assess whether the data are reliable for research purposes and whether the prevalence of medication use can be estimated reliably. In addition, we evaluated the association of misreporting with gender, education and marital status.

Methods

The Northern Finland 1966 Birth Cohort (NFBC 1966)

The Northern Finland 1966 Birth Cohort (NFBC 1966) is based upon live-born children ($N = 12\,058$) in the Finnish provinces of Oulu and Lapland with an expected date of birth during 1966 (Rantakallio, 1969). Altogether 11 636 cohort members were alive at the beginning of 1997. Data on the biological, socio-economic and health conditions, living habits and family characteristics have been collected prospectively since pregnancy. Permission to gather data was obtained from the Ministry of Social and Health Affairs and the study has been approved by the Ethical Committee of the Northern Ostrobothnia Hospital District in Oulu, Finland.

Pharmacy data

The pharmacy data contained the reimbursed physician-prescribed drugs purchased during 1997 and were collected from the register of the Social Insurance Institution (SII) of Finland. Drugs were identified according to the Anatomical Therapeutic Chemical (ATC) classification system (Guidelines for ATC classification, 1990). In the ATC system, drugs are classified according to the organ or system on which they act and their chemical, pharmacological and therapeutic properties. Our data consisted of information on the ATC codes and the date of drug purchase, but not the doses or amount. The selected categories were antipsychotics (N05A), antidepressants (N06A), antiepileptics (N03A), antidiabetics (A10) and beta-blocking agents (C07).

The SII register can be assumed to be comprehensive, having full coverage of the reimbursed medication. Even though some drugs are not entitled to compensation due to low price, drugs for severe chronic diseases are entitled

to full compensation (Haukka *et al.*, 2007). All Finnish citizens have a personal social security number and a social security card. Reimbursement is received if the patient registers at the time of the purchase by showing the social security card.

SR data

A field survey was planned in order to study physical and mental health and their associates in the NFBC 1966. A postal questionnaire was sent to all cohort members during the year 1997 (Haapea *et al.*, 2008). Addresses were retrieved from the population register centre by using the social security number. The cohort members living in northern Finland or in the Helsinki area were also invited to a clinical examination in local health centres or hospitals.

A postal questionnaire was sent to 11,540 cohort members (Figure 1). The mailing was repeated twice if needed. Altogether 7625 (66%) subjects returned the questionnaire by 31 January 1998. All the cohort members were asked to sign an informed consent attached to the postal questionnaire to allow the data collected on them to be used in further research and to allow additional information to be collected from various registers.

The questionnaire consisted of questions on physical and mental health, and on living habits. Specifically, medication use was inquired by asking whether subjects used medications for the indications listed (e.g. headache, depression) with multiple choices: 'not at all', 'occasionally' and 'regularly or continuously'. The subjects were also asked to name the drugs they used currently with the dosage of the drugs, and whether the drugs were prescribed by a physician. An experienced senior psychiatrist (MJ) reviewed and categorized the drugs according to the ATC classification.

Selection of data

The dates of returning the questionnaire ranged widely during 1997 and 1998. As the register contained drugs purchased during 1997, we selected to this study the subjects who returned the questionnaire by 31 January 1998.

The reimbursement by the SII covers a maximum of three months' use of drugs per purchase. We accepted prescription drugs purchased no earlier than six months before the estimated date of filling in the questionnaire. The six-month gap was also used by, for example, Haukka *et al.* (2007) in their study. Also other time windows have been used, e.g. 'legend time', which is calculated by duration of use of prescription, 30-day fixed, and 90-day fixed (e.g. Lau *et al.*, 1997; Nielsen *et al.*, 2008). Lau *et al.* (1997) found better agreement for legend time and 90-day fixed methods than for 30-day fixed method.

We selected antipsychotics and antidepressants as major psychoactive medications, and antiepileptics, antidiabetics and beta-blocking agents as comparators for self-reporting activity. We selected antiepileptics as they are used also as mood stabilizers, and antidiabetics and beta-blocking agents, as they are used for chronic illnesses. The prevalence of these drugs was expected to be about 1–3%.

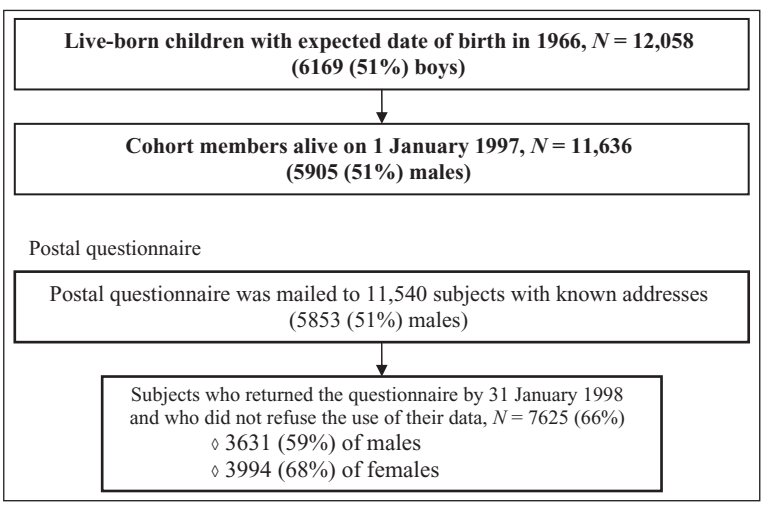

Figure 1 Data collection in a survey conducted in 1997 in the NFBC 1966, and inclusion of subjects in the study of self-reported medication use.

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Socio-economic data

Marital status was inquired in the questionnaire, and it was classified as married or cohabiting versus single, divorced or widowed. Information on education was collected from Statistics Finland. Education at the end of 1997 was divided into secondary (10 to 12 years) or tertiary (over 12 years) versus basic (9 years or less) level.

Statistical methods

We evaluated the prevalence of medication use for SR and pharmacy data separately. The agreement between the SR and pharmacy data was evaluated using Cohen's kappa (κ) (Cohen, 1960), prevalence-adjusted and bias-adjusted kappa (PABAK) (Byrt *et al.*, 1993) and the proportion of positive agreement P_{pos} (Fleiss, 1981). We also present the prevalence index (PI) and bias index (BI) to assess the distribution of medication use (prevalence) and systematic differences (bias) between SR and pharmacy data (Byrt *et al.*, 1993). The calculation of the agreement statistics is presented in the Appendix.

Kappa and PABAK may be interpreted e.g. as follows: <0.20 as slight, 0.21–0.40 as fair, 0.41–0.60 as moderate, 0.61–0.80 as substantial, and >0.80 as almost perfect agreement (Landis and Koch, 1997). PI and BI range from −1 to 1. The PI equals zero when the observed agreement equals 50%, negative when the prevalence is less than 50% and positive when the prevalence is greater than 50%. The BI equals zero if the marginal proportions are equal, i.e. $f_1 = g_1$ and $f_2 = g_2$. A negative BI indicates a higher proportion of medication users from SR data and a positive BI indicates a higher proportion of users from pharmacy data. It has been shown that when prevalence increases κ decreases and when bias increases κ increases (Byrt *et al.*, 1993). The P_{pos} is more suitable than normal agreement percentage when there are many negative responses, i.e. those who did not purchase drugs or report medication use. The value of P_{pos} can be considered analogous to sensitivity (Cicchetti and Feinstein, 1990), ranging from zero to one. Values close to unity signify good agreement and values close to zero poor agreement.

Logistic regression was used to evaluate the association between socio-economic factors and the congruence between the two data sets. Congruence was coded as: 0 = Both SR and pharmacy data indicated the medication was present or both indicated it was absent, 1 = Only one of the sources indicated presence of medication use. The effect of participation was analysed comparing relative risks (RR) and their 95% confidence intervals (CIs) between participants and non-participants. WINPEPI (PEPI-for-Windows) was used to calculate the agreement statistics and the relative risks (Abramson, 2001). SPSS 15.0 was used to perform other statistical analyses.

Subjects may have purchased a drug inside or outside the accepted six-month time window. The latter stands for the purchase happening either after filling in the questionnaire or more than six months prior to it. In such cases, positive SR data was defined as false, and negative SR data as correct. We used the earlier of the dates of informed consent or a clinical examination as a date of filling in the questionnaire.

Results

Prevalences

According to the SII register (pharmacy data), 699 (6.0%) out of the 11,636 cohort members had purchased at least one of the medications selected to this study during 1997. The proportion in our sample (i.e. the cohort members who returned the questionnaire by 31 January 1998) was lower (n = 326, 4.3%). The corresponding figures for the psychoactive medications (N05A or N06A) were 406 (3.5%) in the pharmacy data in all subjects versus 140 (1.8%) in our sample.

Out of 7625 subjects, 72 had purchased antipsychotics, 117 antidepressants, 54 antiepileptics, 54 antidiabetics and 77 beta-blockers. The corresponding figures were 65, 87, 55, 57 and 95 in the SR data (Table 1). The congruence was highest for antidiabetics (κ = 0.92, PABAK = 1.00) and lowest for beta-blockers (κ = 0.55, PABAK = 0.98). The congruence was substantial for antipsychotics (κ = 0.77, PABAK = 0.99) and antidepressants (κ = 0.68, PABAK = 0.98), and almost perfect for antiepileptics (κ = 0.84, PABAK = 1.00) (Table 2).

Socio-economic factors

Gender did not affect the reliability of psychoactive medication (Table 3). Compared to women, men reported the use of beta-blocking agents considerably better [odd ratio (OR) of discordance = 0.53, 95% CI = 0.32 − 0.86]. The congruence between the two data sets was especially poor for women; 27% under-reported and 46% over-reported their use (data not shown). Both men and women reported the use of antidiabetics accurately.

Subjects with secondary or tertiary education reported the use of antidepressants (OR = 1.95, 95% CI = 1.03 − 3.70) and antiepileptics (OR = 7.67, 95% CI = 2.43 − 24.2) better than those with basic education. Married subjects reported the use of antipsychotics (OR = 3.36, 95%

Table 1 Medication use: SR and pharmacy data within our sample and pharmacy data on all subjects in the NFBC 1966

		Responders[1]		All cohort members[2]
Medication	ATC	SR data *n* (%)	Pharmacy data *n* (%)	Pharmacy data *n* (%)
Antipsychotics	N05A	65 (0.9)	72 (0.9)	170 (1.5)
Antidepressants	N06A	87 (1.3)	117 (1.1)	297 (2.6)
Antiepileptics	N03A	55 (0.7)	54 (0.7)	95 (0.8)
Antidiabetics	A10	57 (0.7)	54 (0.7)	94 (0.8)
Beta-blocking agents	C07	95 (1.2)	77 (1.0)	174 (1.5)

Note: ATC, Anatomical Therapeutic Chemical classification system.
[1] Subjects who returned the postal questionnaire by 31 January 1997 ($N = 7625$).
[2] All the cohort members alive in the beginning of January 1997 ($N = 11\,636$).

Table 2 Congruence of the SR and pharmacy data on medication use in the NFBC 1966

Medication	Total	P_{pos}	PI	BI	PABAK	κ (95% CI)
Antipsychotics	84	0.774	98.2%	0.1%	0.99	0.77 (0.69–0.85)
Antidepressants	134	0.686	97.3%	0.4%	0.98	0.68 (0.61–0.76)
Antiepileptics	63	0.844	98.6%	0.0%	1.00	0.84 (0.77–0.92)
Antidiabetics	60	0.919	98.5%	0.0%	1.00	0.92 (0.87–0.97)
Beta blockers	124	0.558	97.8%	0.2%	0.98	0.55 (0.46–0.64)

Note: Total refers to the subjects who reported using the particular drug or had purchased it; P_{pos} is the proportion of positive agreement; PI is the prevalence index; BI is the bias index; PABAK is the prevalence and bias adjusted kappa; κ (95% CI) is Cohen's kappa (95% confidence interval).

CI = 1.62 − 6.97) and antidepressants (OR = 2.89, 95% CI = 1.75 − 4.77) more accurately than those who were not married. Level of education or marital status did not affect the reporting of antidiabetics and beta-blocking agents (Table 3).

Effect of non-participation

Non-participants, i.e. those who did not return the questionnaire by the specified time, had purchased antipsychotics (RR = 1.9, 95% CI = 1.4 − 2.6) and antidepressants (RR = 1.4, 95% CI = 1.1 − 1.8) more commonly than the participants (Table 4).

Discussion

Main results

The reliability of SR data on psychoactive medication use was substantial in our data. The agreement was generally highest for the use of antidiabetics and lowest for the use of beta-blocking agents. Gender did not affect the reliability of psychoactive medication, and the effect of education and marital status varied within psychoactive medication.

Gender has not been associated with drug recall, which is concordant with our results (van den Brandt *et al.*, 1991; West *et al.*, 1995). In our study, however, beta-blocker use was more accurately reported by men. Subjects with higher household income and married subjects have been shown to have better recall than those with lower household income and single, widowed or divorced subjects (Cotterchio *et al.*, 1999). In our study, the effect of education and marital status was similar for psychoactive drugs, but they had no effect on the precision of antidiabetics or beta-blocking agents.

Effect of non-participation

Previous studies have shown that healthy subjects participate in surveys more actively than subjects with poorer

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Table 3 Effect of socio-demographic factors on discordance between the SR and pharmacy data on medication use in the NFBC 1966

	Antipsychotics		Antidepressants		Antiepileptics		Antidiabetics		Beta-blocking agents	
	N	OR (95% CI)	*N*	OR (95% CI)	*N*	OR (95% CI)	*N*	OR (95% CI)	*N*	OR (95% CI)
Gender										
Women	41	1	73	1	31	1	29	1	70	1
Men	43	1.07 (0.52–2.21)	61	0.92 (0.56–1.52)	32	1.62 (0.48–5.49)	31	0.98 (0.24–3.98)	54	0.53 (0.32–0.86)*
Education										
>9 years	64	1	110	1	44	1	55	1	105	1
≤9 years (basic)	20	1.99 (0.81–4.93)	24	1.95 (1.03–3.70)*	19	7.67 (2.43–24.2)*	5	2.91 (0.58–14.7)	19	0.86 (0.37–1.99)
Marital status										
Married	15	1	42	1	21	1	24	1	46	1
Not married	69	3.36 (1.62–6.97)*	92	2.89 (1.75–4.77)*	42	3.04 (0.95–9.72)	36	1.50 (0.35–6.37)	78	1.31 (0.80–2.17)

Note: not married refers to single, divorced or widowed; OR (95% CI) = odds ratio (95% confidence interval).
*Indicates the statistically significant odds ratio.

health. For example, among subjects with psychosis the most severely ill tend to drop out (Lundberg *et al.*, 2005; Haapea *et al.*, 2007). This is in concordance with our results of having a lower proportion of medication use in our sample than in the pharmacy data in the whole cohort. We found a significant difference between the proportions of using antipsychotics or antidepressants between participants and non-participants. Cotterchio *et al.* (1999) have also discussed the effect of non-participation in their study on the accuracy of antidepressant use. They stated that a slightly higher proportion of non-participants reported antidepressant use compared to participants.

Methodological issues

Some of the discordance may be due to the structure of the questionnaire. When planning a survey one should be explicit in inquiring for data. We asked whether subjects used medication currently. For some people current medication use may mean strictly the regular use of a drug at a specified time point, whilst for others having a prescription to be used if needed is enough.

Type of medication may affect the reliability of SR data. For instance, antidiabetic use may be reported accurately because antidiabetics are needed daily on a long-term basis. However, beta-blocking agents are used for asymptomatic chronic illness. Subjects may use them occasionally, on a per-need basis, and therefore not consider them as medication 'used currently' at the time of the inquiry. It may also be that beta-blocking agents are too cheap to be entitled to compensation (and hence do not appear in the pharmacy data) but the users presumably still report using them.

According to Klungel *et al.* (1999), the accuracy of data was better for questions about drugs used for a specific indication than for open-ended questions. It would be useful to use e.g. the ATC system to classify drugs already when preparing the questionnaire. If a subject recalls the use of a specified class of drugs, the name and dose of the drug and the duration of the use can be inquired in more detail. In our study the subjects were asked for medication use for some listed indications, but names of the possible drugs were not given. We inquired for current medication use, hence no time-based recall bias should exist (West *et al.*, 1995). Nielsen *et al.* (2008) noted fixed-time method better than legend time in capturing the use of in-need medications.

The results based on personal interview are likely to be more accurate than questionnaires; for example, Haukka *et al.* (2007) reported kappa values of 0.88 for

Table 4 Medication use in the NFBC 1966 by participation status, i.e. the subjects who returned the questionnaire by specified time versus the subjects who did not. The pharmacy data has not been corrected by the dates of purchase and SR data in this analysis

Medication	Participants, *N* (%)	Non-participants, *N* (%)	RR (95% CI)
Antipsychotics	85 (1.1)	85 (2.1)	1.90 (1.41, 2.56)
Antidepressants	170 (2.2)	127 (3.2)	1.42 (1.13, 1.78)
Antiepileptics	57 (0.7)	38 (0.9)	1.27 (0.84, 1.91)
Antidiabetics	58 (0.8)	36 (0.9)	1.18 (0.78, 1.79)
Beta blockers	111 (1.5)	63 (1.6)	1.08 (0.79, 1.47)
Total	7625	4011	

Note: *N* (%) = number (proportion); RR (95% CI) = relative risk (95% confidence interval).

antipsychotics and 0.77 for antidepressants based on interview. However, according to the literature summery by Garber *et al.* (2004) questionnaires and diaries were more likely to be highly concordant with non-SR-measures than interviews. There are also ways of improving recall in questionnaires or interviews. The most commonly used drugs for specific indications can be listed or photographs of them can be shown as examples (Boudreau *et al.*, 2004; Cotterchio *et al.*, 1999). A calendar of life events can also be used to improve recall (Boudreau *et al.*, 2004).

Even though the subjects reported the use of psychoactive medication accurately, some of them may have been reluctant to report their use. People may either be reluctant to report the use of psychoactive drugs, or the psychological indication itself may lead to poor recall (van den Brandt *et al.*, 1991; Cotterchio *et al.*, 1999). Nielsen *et al.* (2008) suspected possible 'self-stigmation' on self-reporting of antipsychotic medication, but they found no indication on such. Guénette *et al.* (2005) emphasized the confidentiality of collection of SR data in order to avoid over-reporting due to 'social desirability bias'. The confidentiality of SR data, however, also diminishes the under-reporting due to self-stigmation.

Strengths and limitations

Haukka *et al.* (2007) have suggested that medication use is rarely over-reported. In our study some of the subjects reported using medication, e.g. beta-blocking agents, but had no data on their purchase. Part of the over-reporting may be explained by beta-blockers not being entitled to compensation. Some of the over-reporting may be due to time window of addressing SR data to pharmacy data. In addition, although unlikely in this study, there may be a small proportion of people who are misusing drugs or who are otherwise unwilling to register their drug use. They are hardly likely to report their use in questionnaires either. However, considering the large number of subjects studied in the cohort, the over-reporting is minimal.

We had a possibility to make use of extensive pharmacy data by linking it individually to SR data. We had no information on the dose or amount of the medication purchased in the pharmacy data, so we were not able to estimate the duration of prescription. Due to this, we were not able to use all the information from the questionnaire in which the subjects had also reported the dosage of the drugs they reported using. We had to make assumptions about subjects using the drugs for a certain time period and about their state of medication use at the time of filling in the questionnaire. In addition, the pharmacy data only gives information about drug purchase; we do not know whether the drugs were actually consumed.

The date of filling in the questionnaire was not necessarily accurate. We used the date of either informed consent or clinical examination (i.e. the second part of the health survey). Subjects may have filled in the questionnaire long before returning the consent or before attending the clinical examination, which is why we allowed the six-month gap between the dates of purchase and assumed filling in of the questionnaire. This may have caused discordance between the SR and pharmacy data, but it also caused some uncertainty about the true state of medication use.

Drugs were selected using the ATC system. Even though our primary interest was on psychoactive medication, we could not necessarily be sure of whether certain drugs were used for psychiatric disorders. Antiepileptics, for example, are mainly used for treating epilepsy, but they are also used as mood stabilizers for the treatment of bipolar disorder. The new antidepressants may also be

used for other disorders besides depression. Kwon *et al.* (2003) stated that SR data identify antidepressants used primarily for depressive disorders, whereas pharmacy data classify antidepressants by their antidepressant effects. According to Brown *et al.* (2007), SR data are useful in estimating the prevalence of a disorder (hyperlipidemia), but may overestimate the actual use of medication (lipid lowering drugs). Since we compared the medication use classified according to the ATC codes, this should not cause discrepancy in any direction.

Conclusion

The data collected by postal questionnaire can be assumed accurate enough for study purposes, even though it may underestimate the prevalence of medication use due to non-participation. Special attention should be paid to the structure and phrasing of questions during the design phase of the study in order to cover the area of interest explicitly.

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Declaration of interest statement

The authors have no competing interests.

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Appendix

The agreement statistics can be calculated simply from a four-fold table of the form

		Pharmacy data		
		+	−	Total
SR	+	a	b	f_1
data	−	c	d	f_2
Total		g_1	g_2	N

where '+' indicates for presence of medication use, and '−' for absence of medication use.

The proportions of observed agreements (p_o) and expected agreements (p_e) are calculated as $p_o = (a + d)/N$ and $p_e = (f_1 \times g_1 + f_2 \times g_2)/N^2$. Kappa ($\kappa$) can then be calculated as $\kappa = (p_o - p_e)/(1 - p_e)$.

Prevalence index (PI) is estimated as $PI = (a - d)/N$ and bias index (BI) as $BI = (b - c)/N$.

In order to compute prevalence-adjusted and bias-adjusted kappa (PABAK), we replace b and c by their average, $m = (b + c)/2$, and a and d by their average, $n = (a + d)/2$. PABAK can then be computed by $PABAK = [(2n/N) - p_e]/(1 - p_e)$.

Proportion of positive agreement is calculated as $P_{pos} = 2a/(f_1 + g_1)$.

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