

# Repeat prescriptions: refill adherence in relation to patient and prescriber characteristics, reimbursement level and type of medication

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**Background:** Repeat prescribing used in long-term pharmacotherapy is often associated with inadequate patient medication, including non-adherence. In this paper we explore patients' drug refill adherence with repeat prescriptions and relate refill data to patient age and gender, type of prescriber, type of prescribed drug, and reimbursement level. **Methods:** During one week of 2002, copies of 3636 repeat prescriptions filled at 16 large Swedish pharmacies were collected. Satisfactory refill adherence was defined as dispensed refills covering 80–120% of the prescribed treatment time. Under- and oversupplying were defined as <80% and >120% coverage, respectively. **Results:** The average level of refill adherence was 57%, and the level of under- and oversupplying 21% and 22%, respectively. There was no gender difference. Patients who were exempt from payment had higher oversupplies than others (33% versus 19%), and patients of general practitioners had higher refill adherence than patients of hospital physicians. The highest refill adherence was observed for contraceptives (81%) and the lowest for anti-asthmatics, proton pump inhibitors and non-steroidal anti-inflammatory drugs (30–40%). **Conclusions:** Refill non-adherence includes both under- and oversupplying and may vary due to different attitudes between prescribers and between patients. Different therapeutic indications and reimbursement systems are other apparent causes. These observations should be considered in programs aiming to assist patients in following medication prescriptions.

**Keywords:** oversupply, refill adherence, repeat prescriptions, undersupply

Long-term pharmacotherapy is usually carried out using repeat prescriptions. This mode of prescribing has advantages and disadvantages. Drug refills without renewed consultation are convenient for patients and prescribers alike, but several problems may also ensue, as recently reported.<sup>1</sup>

Repeat prescribing might be associated with inadequate patient medication, including non-adherence.<sup>1,2</sup> Medication reviews by pharmacists can reduce the drug-related problems associated with repeat prescriptions.<sup>1,3</sup> Adherence to prescribed medication is important for patients' health, and a Cochrane review<sup>4</sup> showed that patient outcome may be improved following interventions that promote adherence.

Activities to assist the patients in better following of medication prescriptions should preferably be based on knowledge of the level of non-adherence. However, measuring adherence is complicated and all available methods have disadvantages.<sup>5</sup> Estimation of adherence based on refill of repeat prescriptions is a comparatively convenient method.<sup>6</sup> Such data not only show how the patients have their drug supply refilled, they may also indicate the total therapeutic adherence, as shown by several authors.<sup>6–8</sup> Refill adherence data compare favourably with adherence data obtained using alternative methods.<sup>6</sup>

In order to be able to design future effective interventions to improve adherence, we wished to estimate adherence among Swedish patients in relation to different influencing factors using refill adherence data. We have therefore explored how

patients had their repeat prescriptions filled and have related refill data to patient age and gender, type of prescriber, type of prescribed drug, and reimbursement level.

## Methods

All Swedish pharmacies belong to one organization, Apoteket AB (the National Corporation of Swedish Pharmacies), presented elsewhere.<sup>9</sup> The prescription identifies the drug, its strength, amount and dosage as well as the prescriber, and it is valid for 1 year from the date of issue.<sup>10</sup> The prescriber must indicate on the prescription form the number of times the prescription may be dispensed. The same prescription form may thus be used for multiple dispensings without visiting the doctor. At the pharmacy, computer-generated information concerning date of dispensing and amount of drug dispensed is transferred to the prescription form each time the prescription is filled. In the present study the repeat prescriptions included were those that had been dispensed at least twice.

For long-term medication, prescriptions are commonly issued for 1 year of treatment, with 3-month dispensation intervals. Swedish physicians, dentists (included dental hygienists), nurses and midwives have the right to prescribe. For the latter three groups, prescribing is restricted to certain types of drugs.

When a repeat prescription has been filled the maximum number of times prescribed, the prescription is retained at the pharmacy. The patient pays the full cost of drugs up to 900 SEK (approximately €100 or US\$125) during a 12-month period, and is exempt from further payment above 1800 SEK per year.

## Data collection

The study was performed in the southern Swedish County of Jönköping, where drug utilization approximately equals the Swedish average.<sup>11</sup> The county has a population of 328 000

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inhabitants, which is 4% of the Swedish population. It comprises 13 municipalities with 35 health-care centres, three hospitals and 33 pharmacies (information regarding the county of Jönköping is available at <http://www.lj.se>).

During one week of November 2002, repeat prescriptions that had been dispensed at least twice were collected at the 16 largest pharmacies in the county. Pharmacy staff were instructed to make photocopies of both sides of the prescription form and send the copies to the research group.

Collected data included patient age, gender, exemption from payment, drug name and ATC code, date of issue, type of prescriber and prescribed days of treatment. The dates of the dispensings and the amount of drug dispensed each time were also registered. From these data the actual number of days between each fill could be calculated, to be compared with prescribed days of treatment. The identities of the patients remained confidential.

### Definition of refill adherence

Satisfactory refill adherence was defined as dispensed refills covering 80–120% of the prescribed treatment time.<sup>12</sup>

$$\begin{aligned} \text{Satisfactory refill adherence} &= \frac{\text{no. prescribed treatment days/} \\ &\quad \text{no. days between fills} \times 100}{=} \\ &= 80\text{--}120\% \end{aligned}$$

Ideally, a patient would buy a drug for a treatment of 100 days with an interval between two refills of 100 days (refill adherence = 100%). A divergence from prescribed treatment time below –20% indicates treatment gaps and above +20% means drug stockpiling or oversupply. In the following, refill adherence levels <80% are referred to as undersupply and those >120% as oversupply. For each prescription the refill adherence was analysed as shown in figure 1, to evaluate how each patient had the drug supply refilled over time.

### Data analyses

The distribution of refill adherence was analysed in relation to patient age, gender and exemption from payment, and also in relation to type of prescriber and type of drug.

### Statistical analyses

Z-tests were used to determine the statistical significance of the differences between the mean values of adherence related to patient and prescriber characteristics, type of drug and reimbursement level.

## Results

The 16 participating pharmacies dispensed 27 434 prescriptions during the week of data collection. The number of copies of

repeat prescriptions included in the study was 3636, i.e. 13% of the total number of dispensed prescriptions of the participating pharmacies. The included prescriptions had generated 10 844 pharmacy dispensations during the preceding 3–12 months that they had been used by the patients. The number of intervals between two separate dispensations was 7208. Ten days or more had elapsed between issue date and first fill of one-third (34%) of the prescriptions.

The refill adherence for different patient age groups is shown in table 1, and the distribution of the collected prescriptions in relation to the adherence levels is shown in figure 2. The result is an approximately bell-shaped curve. A total of 2058 (57%) prescriptions had a satisfactory refill adherence level, i.e.  $100 \pm 20\%$  (table 1), 762 prescriptions <80% and 816 prescriptions >120%. This is an approximate ratio of 1:3:1.

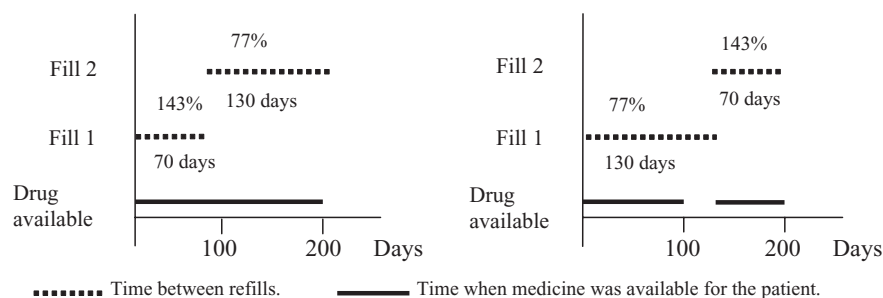
The number of prescriptions increased with patient age up to 70–79 years and then declined. The highest adherence (66%) was seen among very old patients ( $\geq 90$  years of age). Among 40 to 89-year-old patients, 55–60% had satisfactory refill adherence. Adherence was lower among those aged 30–39 years (49%). The youngest patients (<30 years of age) had too few prescriptions to allow reliable evaluation of refill adherence.

There were more prescriptions for female (60%) than for male (40%), but no gender difference in refill adherence were seen (57% versus 55%;  $P = 0.2$ ). However, men had more oversupplies (25%) than women (21%;  $P < 0.001$ ), and fewer undersupplies (20% versus 22%;  $P = 0.04$ ).

More women (448; 56%) than men (358; 44%) were exempt from payment. Patients with full exemption had lower refill adherence (51%) than those without exemption (58%;  $P < 0.001$ ). This was mostly due to oversupply. There were 33% oversupplies among patients with full exemption and only 19% among those without exemption ( $P < 0.001$ ). Conversely, undersupply was lower (16%) in the exempt group than in those without exemption (22%;  $P < 0.001$ ).

Patients with prescriptions from nurses and midwives had the highest refill adherence (94%), whilst the lowest adherence was seen among those who had prescriptions from company-based physicians (44%) (table 2). Patients with prescriptions from general practitioners (GPs) had higher refill adherence than those with prescriptions from hospital physicians, and it was higher among those with prescriptions from private than from publicly employed GPs. Patients visiting chief physicians had higher refill adherence than those seeing other hospital physicians. Repeat prescriptions from dentists were too few to allow evaluation of refill adherence ( $n = 17$ ).

The highest refill adherence in relation to type of medication was 81% (hormonal contraceptives for systemic use) and the lowest was 20% (anti-dementia drugs) (table 3). Contraceptives predominated among the former and were mostly prescribed by midwives. Much lower refill adherence was recorded for inhalation anti-asthmatics (adrenergic anti-asthmatics 43%, others 34%), proton pump inhibitors (39%) and COX-2 inhibitors (23%).



**Figure 1** Evaluation of refill adherence of a prescription with 100 days prescribed treatment time. The patient in the left panel is adherent, i.e. s/he has medicine available during the whole 200 days period, whereas the patient in the right panel is non-adherent because s/he has a gap of 30 days in the middle of the period

Table 1 Refill adherence for patients in different age groups

Patient age group (years)	No. prescriptions [total (%)]	Prescriptions with satisfactory refill adherence (%)	Prescriptions with undersupplies <sup>a</sup> (%)	Prescriptions with oversupplies <sup>b</sup> (%)
0–9	1	100	0	0
10–19	33 (1)	30	15	55
20–29	52 (1)	71	25	4
30–39	136 (4)	49	29	22
40–49	242 (7)	55	27	17
50–59	553 (15)	60	21	18
60–69	859 (24)	56	18	27
70–79	1027 (28)	57	22	21
80–89	654 (18)	55	20	26
90–	79 (2)	66	19	15
Total	3636	57	21	22

a: refill adherence &lt;80%

b: refill adherence &gt;120%

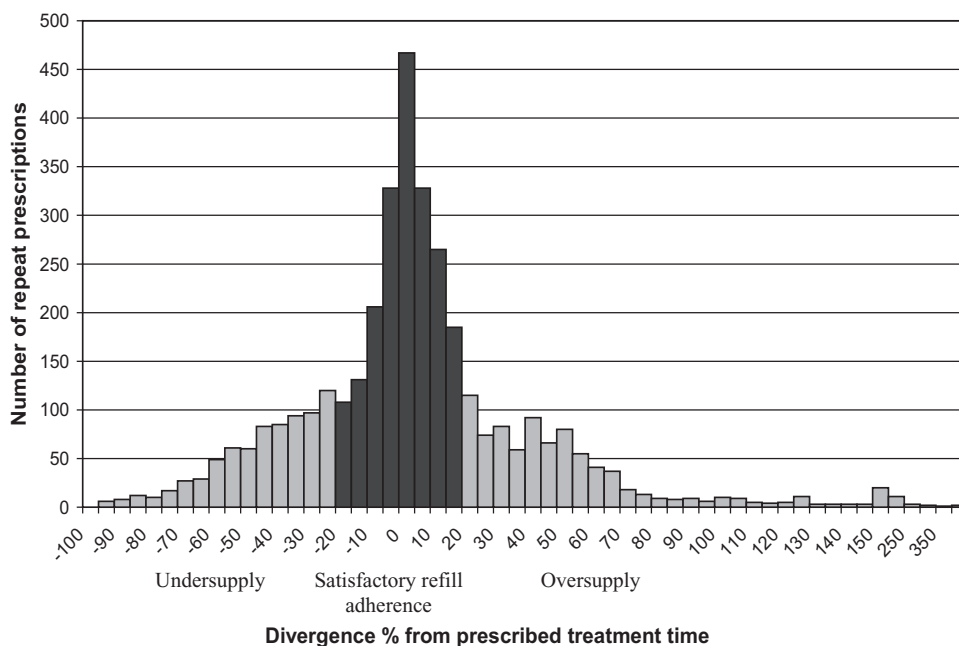


Figure 2 Distributions of repeat prescriptions in relation to refill adherence. Black bars represent prescriptions with satisfactory refill adherence

## Discussion

Repeat prescriptions are intended for patients on long-term medication. The adherence among these patients has been estimated to 50% or less.<sup>13</sup> Complete analysis of a patient's utilization of repeat prescriptions would necessitate comparison of prescriber records with the actual dispensations to the patients. We only had access to the latter. However, British and Swedish studies indicate that 10–20% of repeat prescriptions never reach a pharmacy.<sup>14,15</sup> Accordingly, underutilization of repeat prescriptions is likely to be higher than appears from the current data on refill non-adherence, providing that the patients used only one prescription for the same drug at the same time.

The county of Jönköping was selected for the study since the level of prescribing in this county is close to that of Sweden as a

whole. The month of November was chosen because the drug sales this month are close to one-twelfth of the sales for the whole year. We therefore consider that our sample of repeat prescriptions is representative for the country. All data were collected prospectively, i.e. we assessed not only repeat prescriptions dispensed the maximum number of times (which are the only repeat prescriptions stored at the pharmacies) but also those still open to more dispensations. This should allow a more appropriate measure of refill adherence than a study using only retrospective collection of dispensing data. Apoteket AB (see above) estimates that 40% of prescriptions dispensed at Swedish pharmacies are repeat prescriptions (at least one refill), whereas our sample comprised 13% of all prescriptions reaching the study pharmacies during the study week. This was due to lack of time at some pharmacies to copy all repeat prescriptions. However, the one-third of expected prescriptions that we

**Table 2** Refill adherence in relation to different types of prescribers

Type of prescriber	No. prescription [total (%)]	Prescriptions with satisfactory refill adherence (%)	Prescriptions with undersupplies <sup>a</sup> (%)	Prescriptions with oversupplies <sup>b</sup> (%)
Nurses and midwives	33 (1)	94	3	3
GPs, private <sup>c</sup>	417 (11)	60	17	22
GPs, publicly employed <sup>c,d</sup>	1786 (49)	58	22	20
Chief physicians <sup>d,e</sup>	545 (15)	55	20	25
Other hospital physicians <sup>e</sup>	793 (22)	51	21	27
Dentists	17 (0.5)	47	29	24
Company-based physicians	45 (1)	44	27	29
Total	3636	57	21	22

a: refill adherence &lt;80%

b: refill adherence &gt;120%

c: GPs private versus GPs publicly employed,  $P < 0.001$ d: GPs publicly employed versus chief physicians,  $P < 0.001$ e: chief physicians versus other hospital physicians,  $P < 0.001$ **Table 3** The refill adherence in different types of medicines

ATC code	Type of drug	Number of prescriptions	Prescriptions with satisfactory refill adherence (%)	Undersupply/oversupply (%)
G03A	Hormonal contraceptives for systemic use	42	81	12/7
C01A	Cardiac glycosides	44	75	9/16
H03AA	Thyroid hormones	100	71	13/16
N06AA	Non-selective monoamine reuptake inhibitors	30	67	20/13
C07AB	Beta-blocking agents, selective	307	66	14/21
B01AC	Platelet aggregation inhibitors excluding heparin	285	63	14/22
M04A	Antigout preparations	40	63	20/18
C10AA	HMG CoA reductase inhibitors	212	62	11/27
A10B	Oral blood glucose lowering drugs	87	59	16/25
C09A	ACE inhibitors, plain	136	59	12/29
G03C	Estrogens	161	58	25/17
N06AB	Selective serotonin reuptake inhibitors	101	58	22/20
C03C	Loop diuretics	144	57	22/22
C03A	Thiazides	56	55	27/18
N03	Antiepileptics	51	55	25/20
N05A	Antipsychotics	31	52	32/16
A06	Laxatives	45	51	31/18
C09C	Angiotensin II blockers	67	49	19/31
R03A	Adrenergic anti-asthmatics for inhalation	40	43	23/35
N02A	Opioids	31	42	29/29
A02BC	Proton pump inhibitors	93	39	37/25
M01A	Anti-inflammatory and antireumatic products, non-steroids	67	39	37/24
R03B	Other anti-asthmatics for inhalation	47	34	40/26
M01AH	Coxibs	22	23	41/36
N06D	Anti-dementia drugs	5	20	20/60

obtained should be a large enough sample to permit analysis of refill adherence.

The repeat prescription forms with multiple dispensations noted can be seen as records of the patients' refill adherence behaviour for the last 3–12 months. The fact that the prescription copies were collected at the pharmacies during only one week is therefore of minor importance. The patient identities remained confidential, but it can be assumed that the repeat prescriptions represent separate individuals. Therefore, our data show the number of patients who have a satisfactory refill adherence as well as the number of those who undersupply or oversupply the system. Satisfactory medication adherence is commonly defined as one  $\geq 80\%$ .<sup>16</sup> However, we chose the less common interval of  $100 \pm 20\%$  as satisfactory adherence. It is much less common to indicate an upper level of refill adherence, probably because data on oversupplies are much more difficult to interpret than those on undersupplies. There are, however, reports<sup>12</sup> where  $100 \pm 20\%$  as been used to indicate of 'good compliance'.

One-third of the prescriptions were initially dispensed only 10 days or longer after the date of issue. The corresponding patients may have had drugs available from older prescriptions, but it is also likely that some of these patients actually had therapy gaps and should be part of the refill non-adherence group, which would hence be larger than estimated.

As in previous studies,<sup>17,18</sup> refill adherence tended to be lower in younger and higher in older patients. The gender ratio of repeat prescriptions (60/40 women/men) was similar to the Swedish average,<sup>11</sup> and there was no gender difference in total refill adherence. However, men had higher oversupplies (25%) than women (21%) and women slightly more undersupplies (22%) than men (20%). While small, the latter difference would signify  $\sim 20\,000$  prescriptions in Jönköping county and  $\sim 500\,000$  in the whole of Sweden.

Most probably, undersupply signifies gaps in patients' medicine supply, i.e. periods when the patients do not have medicine available and therefore have no possibility to be adherent. For the patients with oversupplies it is possible that they use too much of the prescribed medicines and in that in a sense they are non-adherent. However, the patients may also be stockpiling medicines, particularly if they are exempt from payment. The proportion of patients with oversupplies was almost twice as high among the patients with full exemption as among those who paid for their medicines (33% versus 19%).

Refill adherence was also dependent on the type of prescriber. As might be expected, a very high adherence was found for prescriptions from nurses and midwives, especially for contraceptives. Prescriptions from private practitioners had a higher refill adherence than prescriptions from publicly employed GPs. Prescription from the former group were associated with higher oversupplies and fewer undersupplies (22% versus 17%) than were the prescriptions from the latter group (20% versus 22%). The seemingly small differences represent large prescription numbers; in the whole of Sweden, oversupplied prescriptions from private GPs would be  $\sim 688\,000$  and undersupplies  $\sim 532\,000$  in 2002. Hence the difference in undersupply and oversupply between private and publicly employed GPs may be clinically relevant.

Prescriptions from chief physicians had higher refill adherence than those from other hospital physicians. Also, these differences represent large number of prescriptions and seem clinically relevant. Reasonably, most chief physicians have longer clinical experience and see more selected patients than the other hospital physicians. All this could influence the refill adherence. The lowest adherence was found for dentists and company-based physicians, but the numbers of observations were few and hence the data are unreliable.

The largest differences in refill adherence were related to different types of medicines, ranging from 81% for

contraceptives to 20% for anti-dementia drugs. Two more groups had refill adherence  $>70\%$  (cardiac glycosides and thyroid hormones). It should be noted that table 3 only lists medicines that are used for long-term treatment. Several important groups of medicines, e.g. antibiotics, do not appear in the table.

Surprisingly, tricyclic antidepressants had a higher refill adherence than selective serotonin reuptake inhibitors, even though the latter are claimed to have fewer side effects, which should favour higher adherence.<sup>19</sup> Another surprising finding was that there was higher refill adherence with selective beta-blockers than with, in turn, ACE inhibitors, loop diuretics, thiazides and AII blockers. Like the antidepressants, the AII blockers have fewer side-effects than other antihypertensives<sup>20</sup> and a better adherence would be expected. The adherence may be influenced by the fact that the selective beta-blockers, ACE inhibitors and loop diuretics may also be given for some other, more symptom-prone indications beside hypertension.

Both non-selective non-steroidal anti-inflammatory drugs and coxibs had a low refill adherence. It is possible that this reflects the fact that pain conditions vary in intensity, making patients liable to vary their intake of these drugs. Anti-asthmatics for inhalation, both adrenergics and corticosteroids, also had low refill adherence; the former apparently being oversupplied and the latter undersupplied. This is in agreement with previous analysis.<sup>13</sup> Another type of medication with low refill adherence and apparent undersupplies was proton pump inhibitors. This might be due to cessation of intake as soon as the stomach discomfort has been alleviated.

## Conclusions

Treatments based upon repeat prescriptions may seem practical but confer major risks of therapeutic failures, refill non-adherence being one reason. This includes both oversupply and undersupply, and may vary due to several factors, among them different attitudes between prescribers and between patients, in the latter case partly related to age and gender. Different therapeutic indications and reimbursement systems are other apparent causes. These observations should be considered in programs aiming to assist patients in following medication prescriptions.

## Acknowledgement

We wish to thank the pharmacies that provided us with the prescription copies.

### Key points

- Patients' refill adherence with repeat prescriptions was examined and related to age, gender, prescriber, drug type and reimbursement level.
- Satisfactory refill adherence was 57% without age or gender difference, the under- and oversupply were 21% and 22%, respectively.
- Patients of GPs had higher adherence than those of hospital doctors.
- Anti-asthmatics, proton pump inhibitors and NSAIDs had the lowest adherence (30–40%).
- Patients exempt from charges had a higher oversupply than others (33 vs 19%).

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