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# How chronic is polypharmacy in old age? A longitudinal nationwide cohort study

#### Running title: The chronicity of polypharmacy

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#### **Impact statement:**

We certify that this novel clinical investigation provides original research about the chronicity of polypharmacy in a large and unselected cohort of older adults. A deeper understanding of the dynamic nature of polypharmacy is an important addition to the current literature.

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# 1 Abstract

2 **OBJECTIVE:** To evaluate the chronicity of polypharmacy among older adults, and to 3 identify factors associated with chronic polypharmacy.

4 **DESIGN:** Longitudinal cohort study using register data.

5 **SETTING**: Nationwide, Sweden.

PARTICIPANTS: All 711,432 older adults (≥65 years) living in Sweden with 5 or more
prescription drugs in October 2010 were included and followed-up until December 2013.
Mean age at baseline was 77 (SD, 7.8) years, 59% were women, and 7% lived in nursing
homes.

MEASUREMENT: Monthly changes in the exposure to polypharmacy. Data regarding
 prescription drug use were extracted from the Swedish Prescribed Drugs Register.

12 **RESULTS:** Overall, 82% were continuously exposed to polypharmacy during  $\geq 6$  months, 13 and 74% during  $\geq$ 12 months. The proportion of individuals who remained exposed until the end of the study was 55%. Among the 21,361 individuals who had not been exposed to 14 polypharmacy during the 6-month period before baseline (i.e. with a new episode of 15 polypharmacy), only 30% remained exposed for  $\geq 6$  months. The proportion of older adults 16 who spent at least 80% of their follow-up time with polypharmacy was substantially higher 17 18 among prevalent polypharmacy users at baseline than among those with a new polypharmacy 19 episode (80% vs 24%, p<0.01). Factors associated with chronic polypharmacy included higher age, female gender, living in an institution, chronic multimorbidity, and multi-dose 20 dispensing. 21

- CONCLUSION: Polypharmacy is most often chronic, although a substantial share of older
   adults experience short, recurring episodes of polypharmacy and are thus exposed to its
   potential harms in a transient rather than persistent manner.
- **Keywords:** duration; drugs; epidemiology; medication; polypharmacy

# 26 Introduction

27 Multimorbidity is common among older adults and often results in multiple medication use. Polypharmacy (commonly defined as the concurrent use of 5 or more drugs)<sup>1</sup> is a concern 28 because it has been linked to an array of negative health outcomes.<sup>2–6</sup> The prevalence of 29 polypharmacy has increased in most countries during the last decades <sup>7-11</sup>. In the United 30 States, it is estimated that about 40% of people aged 65 years or older use >5 drugs 31 concomitantly.7 Yet few studies have documented the longitudinal development of 32 polypharmacy over time, and little is known about the proportion of older adults who are 33 chronically exposed to polypharmacy. Prior studies suggest that older adults tend to persist 34 with polypharmacy over time.<sup>12-16</sup> Factors such as higher age, female gender, high BMI, 35 36 smoking and chronic conditions are associated with higher odds of remaining on polypharmacy.<sup>16</sup> However, these studies were based on survey data with several years 37 38 between each wave. The use of prescription drugs by older adults can fluctuate, and episodes of polypharmacy can occur sporadically. Newly diagnosed chronic conditions and temporary 39 changes in health status (e.g. post-operative pain, infections) can for instance prompt an 40 increase in the number of drugs, while deprescribing and lack of adherence can shorten the 41 medication list. 42

Understanding the chronicity of polypharmacy is important for a number of reasons<sup>17</sup>. First, most definitions of polypharmacy do not consider whether the exposure to polypharmacy is chronic or transient.<sup>18,19</sup> Yet, this has implications for evaluating the quality of drug prescribing since short-term exposure to polypharmacy as a response to acute events is often clinically appropriate. Second, various interventions have been implemented to reduce the

prevalence and the harms of polypharmacy. Most of these interventions have proven 48 unsuccessful.<sup>20,21</sup> Potentially because polypharmacy may not always be a chronic and 49 persistent hazard,<sup>22</sup> making it difficult to provide tailored interventions at the right time for 50 older adults<sup>18</sup>. Third, observational studies aiming at establishing a causal association 51 between polypharmacy and subsequent health outcomes have seldom considered 52 polypharmacy as a time-varying or cumulative exposure based on the assumption that 53 polypharmacy is by definition chronic.<sup>23</sup> Yet, until now, this assumption has remained 54 untested and there exists no consensual definition of what constitutes chronic 55 polypharmacy.<sup>19</sup> Our aim was thus twofold: i) to evaluate the degree of chronicity of 56 polypharmacy among older adults in Sweden, and ii) to identify factors associated with 57 chronic rather than transient polypharmacy. 58

## 60 Methods

#### 61 Study population

We used register data with nationwide coverage in Sweden to create a longitudinal cohort of 62 older adult ( $\geq 65$  years) who were exposed to  $\geq 5$  drugs in October 2010. Study participants 63 were followed prospectively until December 2013, i.e. for up to 37 months. The Swedish 64 Prescribed Drug Register was linked to the National Patient Register, the National Cause of 65 Death Register, and the Social Services Register, as described elsewhere.<sup>24</sup> We excluded 66 individuals who died during the first 12 months of follow-up, as people at the end of life 67 might have specific clinical needs.<sup>25</sup> The selection of the study population is presented in 68 69 Supplementary materials Figure S1.

#### 70 Outcome measurement: polypharmacy

71 Data regarding prescription drug use were extracted from the Swedish Prescribed Drugs Register, which collects information about all prescription drugs delivered in pharmacies in 72 Sweden.<sup>26</sup> Exposure periods were constructed for each dispensed drug based on: (i) the date 73 74 of drug dispensing, (ii) the number of dispensed defined daily doses, and (iii) the prescribed daily dose as reported by the prescriber.<sup>27,28</sup> We then calculated the number of different drugs 75 76 used in each 30-day window, i.e. distinct substances according to the 5th level of Anatomical Therapeutic Chemical (ATC) classification system. As illustrated in Figure S2, individuals 77 were considered as exposed to polypharmacy during a given month when the number of 78 drugs was  $\geq 5$ . 79

80 To distinguish "chronic" from "transient" polypharmacy exposure, we used the different approaches illustrated in Figure 1. Health problems are usually defined as "chronic" when 81 they persist over time without any measurable interruptions (e.g. diabetes, heart failure). To 82 83 reflect this, we calculated the *duration* of polypharmacy as the number of consecutive months spent with  $\geq 5$  different drugs. We considered the first episode, starting at baseline and 84 stopping when the patient was no longer exposed to polypharmacy for at least 2 months. In 85 86 other words, interruptions in polypharmacy exposure were discarded if they lasted  $\leq 1$  month. This 'grace period' was used to reduce the influence of irregular drug refill patterns. 87 88 Chronicity of polypharmacy was calculated as the proportion of individuals who remained 89 exposed for  $\geq 6$  months and  $\geq 12$  months.

90 Other health problems do not persist over time without any measurable interruption, but can still be considered as chronic if people are experiencing them more often than not (e.g. 91 chronic pain, psoriasis). The underlying assumption is that some conditions occur so 92 93 frequently that their impact on people's everyday life is constant although their onset appears as a series of discrete events. In order to mirror this second scenario, we calculated the 94 95 *fraction of time with polypharmacy* by dividing the number of months with polypharmacy 96 (numerator) by the total number of months of available follow-up (denominator). The numerator did include grace periods. We then defined chronic polypharmacy users as older 97 adults who had a fraction of time with polypharmacy  $\geq 80\%$  (e.g. at least 30 months out of 37 98 99 for those surviving the complete follow-up). This is similar to how drug adherence is calculated using the medication possession ratio.<sup>29</sup> 100

101 [Figure 1 about here]

#### 102 Other covariates

103 Living arrangement at baseline was defined as 'community-dwelling' or 'living in 104 institution', using data from the Social Services Register. *Multimorbidity* was assessed using 105 a validated assessment tool (5), which captures 60 distinct chronic diseases using data from 106 the national patient register during the 3 years prior to baseline, as well as data about specific 107 medications dispensed during the same period. This variable was defined as the number of 108 chronic conditions, with  $\geq 5$  conditions as the maximum value. *Multi-dose dispensing* (in Swedish, ApoDos) refers to drugs administered through portion packed plastic pouches. It is 109 110 especially common among older adults living in nursing homes in Sweden.<sup>30</sup>

#### 111 Statistical analysis

We calculated the duration of polypharmacy for each individual, and identified those who 112 remained exposed for  $\geq 6$  and  $\geq 12$  consecutive months. To account for left censoring we 113 114 stratified the population according to their exposure to polypharmacy during the 6-month period before baseline. Since we excluded older adults who died during the first year of 115 follow-up, outcome measurement was not affected by right censoring (i.e. survival). 116 However, the persistence of polypharmacy throughout the entire follow-up was analyzed 117 with Kaplan-Meier survival functions accounting for mortality. We then measured the 118 119 fraction of time with polypharmacy as the number of months spent with polypharmacy divided by the total number of months of available follow-up. The proportion of older adults 120 who had a fraction of time with polypharmacy  $\geq 80\%$  was reported with percentages. Since 121 122 this indicator is proportional to the contributing time of each individual, it is not affected by mortality selection. We analyzed factors associated with a high fraction of time with 123

124 polypharmacy using multivariate logistic regression models adjusted for age, sex, living arrangement, number of chronic conditions, dispensing regimen and number of drugs at 125 baseline. All estimates from the logistic regression are calculated as predicted probabilities 126 127 and presented as percentages (with 95% confidence intervals) using the margins command in Stata version 14.1 (StataCorp, College Station, TX). Predicted probabilities can be compared 128 across models and can be interpreted as adjusted proportions conditional on the covariates.<sup>31</sup> 129 Post hoc, we stratified the analysis by dispensing regimen to investigate the combined effect 130 of living arrangement and dispensing regimen. In sensitivity analyses, the fraction of time 131 132 with polypharmacy was categorized using a lower cut-off value (50% instead of 80%), which has previously been used as a definition of chronic polypharmacy <sup>32</sup> 133

#### 134 Ethical approval

Data were anonymized and the Regional Ethical Review Board in Stockholm approved the
study (2013/1941-31/3 and 2015/1319-32).

### 138 **Results**

139 Out of 1,752,022 older adults (≥65 years) alive at baseline, 769,286 were exposed to polypharmacy. After excluding 57,854 individuals who died during the first 12 months of 140 141 follow-up, the study population thus consisted of 711,432 older adults (Supplementary Figure S1). This represents 44% of the population aged  $\geq$ 65 years in Sweden. Mean age at baseline 142 was 77.4 years (SD 7.8), 59.1% were women. About 3% (n=21,361) of study participants 143 144 started a new episode of polypharmacy, i.e. had not been exposed to polypharmacy during the 6-month period before baseline (Table 1). Persons with a new episode of polypharmacy were 145 on average younger, had fewer chronic conditions and used fewer drugs at baseline (Table 146 147 S1).

148 [Table 1]

149 Polypharmacy was often long lasting. Overall, 82.3% of participants were exposed to 150 polypharmacy for  $\geq 6$  months, and 74.3% for  $\geq 12$  months. Among older adults with a new polypharmacy episode, these proportions were 29.8%, and 18.6%, respectively (Table 2). The 151 proportion of individuals who remained exposed to polypharmacy until the end of follow-up 152 was 55.3% in the total study population, but only 9.3% among people who had not been 153 exposed to polypharmacy before baseline. Among the 317,478 older adults who discontinued 154 polypharmacy, 76.3% experienced at least one more episode of polypharmacy during the 155 follow-up period (Table S2). As shown in Figure 2, polypharmacy persisted for a longer time 156 157 among older adults aged 75 or older than among younger individuals. Episodes of polypharmacy were also longer among individuals with a higher number of medications at 158 baseline (Figure S3). 159

160 [Table 2]

161 [Figure 2]

During follow-up, we observed 21.2 million person-months with polypharmacy out of a total 162 163 of 25.3 million person-months of follow-up. The average fraction of time with polypharmacy was thus 84%, ranging from 80% among individuals aged 65–74 years to 89% among those 164 165 aged 95 years and older. Table 3 shows the proportion of older adults with a high fraction of time with polypharmacy, i.e. exposed to polypharmacy for  $\geq 80\%$  of follow-up. In the total 166 167 study population, 79.9% of older adults had a high fraction of time with polypharmacy, compared with 23.6% among persons with a new polypharmacy episode at baseline. After 168 169 adjustment for potential confounders, this proportion increased with age, as well as with 170 multi-dose drug dispensing compared with ordinary prescriptions (adjusted predicted probability 93% vs 78%, p<0.01). The proportion of nursing home residents with a high 171 fraction of time with polypharmacy was higher than among community dwellers (90.7% vs 172 79.1%). However, after adjustment for other covariates, this association was reversed 173 (predicted probability 76.7% vs. 80.1%). In post-hoc analysis, we explored the interaction 174 175 between living arrangement and drug dispensing scheme. This showed that communitydwellers with multi-dose dispensing were in fact more likely to have a high fraction of time 176 177 with polypharmacy than persons living in institution (Table S3). In sensitivity analyses where 178 the fraction of time with polypharmacy was calculated without the one month grace period which yielded similar numbers, and using a cut-off value of  $\geq$ 50% which left the association 179 with other covariates largely unaffected although a larger proportion of older adults were 180 181 classified as chronic polypharmacy users (Table S4 and S5).

# 183 **Discussion**

This large longitudinal cohort study tracking monthly changes in drug utilization among older adults in Sweden shows that polypharmacy (concurrent use of  $\geq 5$  drugs) is often a chronic state. This was demonstrated with two complementary approaches.

First, when focusing on the *duration* of polypharmacy episodes, our data clearly show that 187 polypharmacy is persistent for a majority of older adults. About 75% of the individuals with 188 189 polypharmacy at baseline remained exposed to polypharmacy for at least 12 consecutive months. Moreover, even though persons with a new polypharmacy episode at baseline were 190 191 more likely to discontinue polypharmacy in the short term, more than three quarters of the 192 people who stopped polypharmacy eventually transitioned back to polypharmacy before the 193 end of the study period. This suggests that polypharmacy is often a chronic state, however a 194 substantial share of older adults experience short episodes of polypharmacy and are thus 195 exposed to its potential harms in a transient rather than persistent manner. This is especially true among those who are prescribed 3 to 4 medications for the management of chronic 196 diseases (and who are likely to fluctuate around the threshold of 5 drugs used to define 197 198 polypharmacy).

Another way to assess the longitudinal exposure to polypharmacy is to investigate the proportion of months that older adults spend with polypharmacy. Contrary to *duration*, which measures the length of continuous and uninterrupted polypharmacy episodes and is therefore particularly sensitive to grace periods and right censoring (e.g. survival), the *fraction of time with polypharmacy* describes the burden of polypharmacy with respect to the available follow-up time. This approach is comparable to the methodology proposed by Franchi et al., 205 for defining chronic polypharmacy users, which consists in measuring the proportion of individuals exposed to polypharmacy at least 6 out of 12 months.<sup>32</sup> In the present study, we 206 found that 80% of older adults had a high fraction of time with polypharmacy (i.e. spent 207 208  $\geq$ 80% of follow-up with polypharmacy), which is indicative of a chronic exposure. Risk factors associated with high fraction of time with polypharmacy included higher age, female 209 gender, living in institution, chronic multimorbidity, and multi-dose dispensing <sup>33–35</sup>. When 210 using the same cut-off value as Franchi et al. $^{32}$  – namely being exposed to polypharmacy 211 during more than 50% of the available months -42% of older adults who started a new 212 213 polypharmacy episode at baseline had chronic polypharmacy in our study. An unexpected finding was that the adjusted probability of spending a large proportion of months with 214 polypharmacy was higher among people residing in the community than in nursing homes. 215 216 However, more detailed analyses revealed that this association was mostly driven by multi-217 dose dispensing – the small share of persons living in the community with multi-dose drug dispensing had the largest fraction of time with polypharmacy. The finding that people with 218 219 multi-dose dispensing spend a higher fraction of time with polypharmacy is in agreement with previous Swedish studies showing that persons with multi-dose dispensing have fewer 220 changes made to their drug regimens (e.g. dose adjustments, drug discontinuations and newly 221 prescribed drugs) <sup>3036</sup>. One suggested reason for the fewer changes is that prescribers have the 222 possibility to renew all drugs at once, which is not possible with ordinary prescriptions  $^{36}$ . 223

There currently exists no consensual definition of polypharmacy, but two aspects have been widely discussed: the number of drugs that defines polypharmacy in a clinically meaningful way,<sup>37,38</sup> and the criteria that would allow for drawing the line between appropriate and inappropriate polypharmacy.<sup>20</sup> These two dimensions – the *intensity* and the *composition* of 228 polypharmacy - are indeed important. However, only few studies have made a distinction between chronic and transient polypharmacy.<sup>19</sup> Our study shows that exposure to 229 polypharmacy is not always stable over time, and that transient polypharmacy episodes are 230 231 not uncommon. The notion of *temporality* should thus be better accounted for in the future. Observational studies that have investigated the association between polypharmacy and 232 negative health outcomes have seldom considered polypharmacy as a time-varying 233 exposure.<sup>2,39</sup> Yet, doing so would considerably improve the assessment of harms of 234 polypharmacy and could potentially elucidate the question whether the effect of 235 236 polypharmacy is cumulative (i.e. longer exposure to polypharmacy leads to an accumulated risk of adverse effects) or if polypharmacy is hazardous even if exposure is short-lasting. The 237 potential cumulative hazard of polypharmacy was recently highlighted in a British study, 238 239 which demonstrated that the associations between polypharmacy and physical and cognitive capabilities was more pronounced among older adults with a long-term exposure to 240 polypharmacy.<sup>23</sup> 241

#### 242 Strengths and limitations

243 The main strength of this study is that it includes the entire population of older adults aged  $\geq$ 65 years with polypharmacy in Sweden, followed up for 3 years. The monthly assessments 244 of polypharmacy exposure provides better time resolution of the fluctuations in 245 polypharmacy status than earlier survey-based studies with longer time periods between 246 survey waves.<sup>12–16,23</sup> There are some notable limitations to the study. First, we assessed 247 monthly exposure to polypharmacy rather than weekly or even daily exposure periods, which 248 249 could overlook some of the fluctuations in drug use. The choice of monthly time windows was dictated by the considerable computation power required to calculate concurrent drug 250

251 exposure for a population of 700,000 individuals over 3 years with a more detailed time resolution. It should also be noted that drugs used in hospitals are not recorded in the Swedish 252 Prescribed Drug Register, and a one-month stay in hospital could thus result in a change in 253 254 polypharmacy because of not filling new prescriptions. Additionally, over the counter drugs are not recorded in the Swedish Prescribed Drug Register, this most likely leads to an 255 underestimation of the individual burden of polypharmacy. Adherence to different 256 257 medications could lead to misclassification of the exposure to polypharmacy in this study: our data do not provide information about drugs that were prescribed but never dispensed or 258 259 whether the dispensed drugs were actually consumed. Our results should be interpreted in the 260 light of this limitation. To reduce the risk of overestimating short-term fluctuations, we only considered polypharmacy to be discontinued if two consecutive months were spent without 261 262 polypharmacy. Second, we calculated the number of drugs by summing together all distinct ATC codes including medications intended for short-term use that do not contribute to 263 chronic polypharmacy. However, considering all prescribed drugs reflects the natural course 264 of polypharmacy in the older population. Fourth, we tried to isolate people with a new 265 episode of polypharmacy at baseline from those who had already been exposed. This is 266 because incident polypharmacy users have been proposed as a promising target for future 267 interventions.<sup>23</sup> However, because we could only construct a 6-month *washout* period before 268 269 baseline, we cannot be certain that these individuals have a truly incident episode of 270 polypharmacy. Last, polypharmacy is often a result of multimorbidity. We were able to account for the number of chronic conditions at baseline. However, future studies should also 271 investigate how severity of different conditions affects chronicity of polypharmacy. 272

In conclusion, in this longitudinal study of more than half a million older people followed for 273 up to three years, we found that that about 75% of the persons with polypharmacy were 274 exposed to polypharmacy for at least 12 consecutive months. A large majority of older adult 275 276 was also exposed to polypharmacy for more than 80% of the total study months. Our results therefore suggest that polypharmacy is most often chronic, but that a substantial share of 277 older adults experience short, recurring episodes of polypharmacy and are thus exposed to its 278 potential harms in a transient rather than persistent manner. This highlights the need to 279 consider polypharmacy as a dynamic state in both epidemiological studies and in clinical 280 281 practice.

282

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Consultant		Х		Х		Х		Х
Stocks		Х		Х		Х		х
Royalties		X		Х		X		Х
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# 313 Supplementary material

314 Brief title: Supplementary analyses of chronicity of polypharmacy

#### 313 **Figure captions**

Figure 1. Fictitious example of two persons followed from baseline until the end of the study 314 period, i.e. for a follow-up time of 37 months in total. Each square represents 1 month. The 315 washout period of 6 months before baseline is used to distinguish persons who were already 316 exposed to polypharmacy before baseline (Person A) from those who started a new 317 318 polypharmacy episode at baseline (Person B). Each episode of polypharmacy starts at the 319 first month of exposure, and ends when the person remains unexposed for at least 2 consecutive months (grace period). In this example, both persons are considered as having a 320 first episode of polypharmacy that persisted for 7 months, followed by 2 other episodes of 321 polypharmacy. The fraction of time with polypharmacy is calculated as the number of 322 323 months with polypharmacy - including grace periods - divided by the total number of 324 months of available follow-up. In this example, the fraction of time with polypharmacy is equal to  $33 \div 37$  (89.2%). Thus, considering a cut-off value of  $\ge 80\%$ , these persons are defined 325 326 as chronic polypharmacy users.

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Figure 2: Kaplan-Meier survival functions. Solid-line curves denotes the persistence of polypharmacy with a 2-month grace period. Dotted-line curves denotes the persistence of polypharmacy with no grace period (sensitivity analysis). Vertical dashed lines indicate polypharmacy exposure at 6 and 12 months, respectively.

Sex, No (%)	001 175 (40 00/)
Men	291,175 (40.9%)
Women	420,257 (59.1%)
Age	
Mean (SD)	77.4 (7.8)
No (%)	
65-74 years	300,810 (42.3%)
75-84 years	273,069 (38.4%)
85-94 years	129,715 (18.2%)
95 years +	7,838 (1.1%)
Living arrangement, No (%)	
Community	658,693 (92.6%)
Institution	52,739 (7.4%)
Number of chronic conditions	
Mean (SD)	3.7 (2.6)
No (%)	
0	41,256 (5.8%)
1	102,904 (14.5%)
2	122,735 (17.2%)
3	116,609 (16.4%)
4	98,338 (13.8%)
≥5	229,590 (32.3%)
Drug dispensing scheme, No (%)	
Ordinary prescription	611,123 (85.9%)
Multi-dose dispensing	100,309 (14.1%)
Number of drugs at baseline	
Mean (SD)	8.0 (3.1)
No (%)	
5	149,247 (21.0%)
6	128,527 (18.1%)
7	105,530 (14.8%)
8	83,972 (11.8%)
9	65,710 (9.2%)
$\geq 10$	178,446 (25.1%)
Polypharmacy during the 6-month	
period before baseline, No (%)	
No	21,361 (3.0%)
Yes	690,071 (97.0%)

**Table 1.** Characteristics of older adults with polypharmacy at baseline (Sweden, 2010)

Death during follow-up, No (%)

Between 12 and 24 months	54,476 (7.7%)
Between 25 and 37 months	57,027 (8.0%)
Survived follow-up	599,792 (84.3%)

	Entire (n=71	e cohort 1,432 )	Older adults with a new polypharmacy episode at baseline (n=21,361)			
	$\geq$ 6 months $\geq$ 12 months		$\geq 6$ months	$\geq$ 12 months		
	%	%	%	%		
Total	82.3	74.3	29.8	18.6		
Sex						
Men	81.8	73.2	31.9	19.9		
Women	82.7	75.0	28.2	17.6		
Age						
65-74 years	78.1	68.5	26.8	15.6		
75-84 years	84.2	76.7	33.0	21.6		
85-94 years	87.8	82.0	36.5	25.6		
95 years +	88.6	83.2	29.5	17.0		
Living arrangement						
Community	81.4	73.0	29.4	18.1		
Institution	93.7	90.5	48.4	37.9		
Number of chronic conditions						
0	65.2	53.3	20.5	11.5		
1	73.2	62.4	25.2	14.7		
2	77.4	67.7	29.9	18.2		
3	81.2	72.2	34.0	21.7		
4	84.8	77.0	36.3	24.2		
≥5	91.7	86.7	44.1	31.5		
Drug dispensing scheme						
Ordinary prescription	80.2	71.2	29.1	17.8		
Multi-dose dispensing	95.5	93.0	51.4	41.8		
Number of drugs at baseline						
5	55.0	41.8	23.4	13.7		
6	76.1	64.3	35.1	21.5		
7	86.7	77.7	46.5	31.2		
8	92.0	85.4	56.2	40.3		
9	95.0	90.2	69.1	56.6		
≥10	97.8	95.5	78.4	67.3		
Death during follow-up						
Between 12 and 24 months	90.5	85.9	43.8	34.6		
Between 25 and 37 months	89.4	84.4	41.6	29.8		
Survived follow-up	80.9	72.3	28.6	17.4		

**Table 2.** Persistence of polypharmacy ( $\geq$ 5 drugs) among older adults in Sweden.

<sup>a</sup> Duration of polypharmacy was calculated as the number of consecutive months with polypharmacy, with a 2-month grace period (see *methods* for more information).

**Table 3.** Proportion of older adults with a high fraction of time with polypharmacy (≥80%) during follow-up

	Entire cohort (n=711,432)			Older adults with a new polypharmacy episode at baseline (n=21.361			
	Crude %	Adjusted %	95% CI	Crude %	Adjusted % <sup>a</sup>	95% CI	
Total	79.9	79.9	(79.8-80.0)	23.6	23.6	(23.1-24.2)	
Sex							
Men	79.3	80.5	(80.4-80.6)	24.5	24.4	(23.6-25.2)	
Women	80.0	79.5	(79.4-79.6)	22.9	23.0	(22.3-23.7)	
Age							
65-74 years	74.8	77.7	(77.6-77.8)	19.5	20.5	(19.8-21.2)	
75-84 years	82.5	81.6	(81.5-81.7)	27.8	27.1	(26.1-28.1)	
85-94 years	86.1	82.7	(82.5-82.9)	33.2	29.4	(27.5-31.2)	
95 years +	85.9	81.1	(80.2-82.0)	31.0	22.3	(15.7-28.8)	
Living arrangement							
Community	79.1	80.1	(80.0-80.2)	23.1	23.4	(22.9-24.0)	
Institution	90.7	76.7	(76.1-77.3)	47.2	29.4	(25.1-33.7)	
Number of chronic conditions							
0	60.6	75.5	(75.2-75.8)	15.3	17.4	(16.1-18.7)	
1	69.5	78.0	(77.8-78.2)	18.7	20.1	(19.0-21.1)	
2	74.4	78.7	(78.5-78.9)	23.8	24.1	(22.9-25.2)	
3	78.5	79.6	(79.4-79.8)	27.1	26.0	(24.6-27.4)	
4	82.8	81.1	(80.9-81.4)	30.8	28.5	(26.6-30.4)	
≥5	90.5	84.1	(83.9-84.3)	37.5	31.8	(29.8-33.8)	
Drug dispensing scheme							
Ordinary prescription	77.8	79.1	(79.0-79.2)	22.7	23.0	(22.4-23.6)	
Multi-dose	92.8	87.9	(87.6-88.2)	50.6	39.9	(35.7-44.1)	
Number of drugs at baseline							
5	51.6	55.8	(55.6-56.1)	19.1	19.5	(18.9-20.2)	
6	72.1	74.1	(73.8-74.3)	26.7	26.4	(25.1-27.6)	
7	83.7	84.2	(84.0-84.4)	35.2	34.2	(32.0-36.5)	
8	90.1	89.8	(89.6-90.0)	41.2	38.0	(34.4-41.6)	
9	93.8	93.3	(93.1-93.5)	61.4	55.3	(49.6-61.0)	
≥10	97.2	96.6	(96.5-96.7)	63.3	56.5	(49.4-63.5)	

<sup>a</sup> Probabilities mutually adjusted for the other covariates in the table.