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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.

**Word count:**

Abstract 244

Full text 2997

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.

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

10 **MEASUREMENT:** Monthly changes in the exposure to polypharmacy. Data regarding  
11 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  
14 end of the study was 55%. Among the 21,361 individuals who had not been exposed to  
15 polypharmacy during the 6-month period before baseline (i.e. with a new episode of  
16 polypharmacy), only 30% remained exposed for  $\geq 6$  months. The proportion of older adults  
17 who spent at least 80% of their follow-up time with polypharmacy was substantially higher  
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  
20 higher age, female gender, living in an institution, chronic multimorbidity, and multi-dose  
21 dispensing.

22 **CONCLUSION:** Polypharmacy is most often chronic, although a substantial share of older  
23 adults experience short, recurring episodes of polypharmacy and are thus exposed to its  
24 potential harms in a transient rather than persistent manner.

25 **Keywords:** duration; drugs; epidemiology; medication; polypharmacy

## 26 **Introduction**

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

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

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

59

## 60 **Methods**

### 61 **Study population**

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

### 70 **Outcome measurement: polypharmacy**

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

80 To distinguish “chronic” from “transient” polypharmacy exposure, we used the different  
81 approaches illustrated in Figure 1. Health problems are usually defined as “chronic” when  
82 they persist over time without any measurable interruptions (e.g. diabetes, heart failure). To  
83 reflect this, we calculated the *duration* of polypharmacy as the number of consecutive months  
84 spent with  $\geq 5$  different drugs. We considered the first episode, starting at baseline and  
85 stopping when the patient was no longer exposed to polypharmacy for at least 2 months. In  
86 other words, interruptions in polypharmacy exposure were discarded if they lasted  $\leq 1$  month.  
87 This ‘grace period’ was used to reduce the influence of irregular drug refill patterns.  
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  
91 still be considered as chronic if people are experiencing them more often than not (e.g.  
92 chronic pain, psoriasis). The underlying assumption is that some conditions occur so  
93 frequently that their impact on people’s everyday life is constant although their onset appears  
94 as a series of discrete events. In order to mirror this second scenario, we calculated the  
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  
97 numerator did include grace periods. We then defined chronic polypharmacy users as older  
98 adults who had a fraction of time with polypharmacy  $\geq 80\%$  (e.g. at least 30 months out of 37  
99 for those surviving the complete follow-up). This is similar to how drug adherence is  
100 calculated using the medication possession ratio.<sup>29</sup>

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  
109 Swedish, *ApoDos*) refers to drugs administered through portion packed plastic pouches. It is  
110 especially common among older adults living in nursing homes in Sweden.<sup>30</sup>

111 **Statistical analysis**

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

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

#### 134 **Ethical approval**

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

137

## 138 **Results**

139 Out of 1,752,022 older adults ( $\geq 65$  years) alive at baseline, 769,286 were exposed to  
140 polypharmacy. After excluding 57,854 individuals who died during the first 12 months of  
141 follow-up, the study population thus consisted of 711,432 older adults (Supplementary Figure  
142 S1). This represents 44% of the population aged  $\geq 65$  years in Sweden. Mean age at baseline  
143 was 77.4 years (SD 7.8), 59.1% were women. About 3% ( $n=21,361$ ) of study participants  
144 started a new episode of polypharmacy, i.e. had not been exposed to polypharmacy during the  
145 6-month period before baseline (Table 1). Persons with a new episode of polypharmacy were  
146 on average younger, had fewer chronic conditions and used fewer drugs at baseline (Table  
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  
151 polypharmacy episode, these proportions were 29.8%, and 18.6%, respectively (Table 2). The  
152 proportion of individuals who remained exposed to polypharmacy until the end of follow-up  
153 was 55.3% in the total study population, but only 9.3% among people who had not been  
154 exposed to polypharmacy before baseline. Among the 317,478 older adults who discontinued  
155 polypharmacy, 76.3% experienced at least one more episode of polypharmacy during the  
156 follow-up period (Table S2). As shown in Figure 2, polypharmacy persisted for a longer time  
157 among older adults aged 75 or older than among younger individuals. Episodes of  
158 polypharmacy were also longer among individuals with a higher number of medications at  
159 baseline (Figure S3).

160 [Table 2]

161 [Figure 2]

162 During follow-up, we observed 21.2 million person-months with polypharmacy out of a total  
163 of 25.3 million person-months of follow-up. The average fraction of time with polypharmacy  
164 was thus 84%, ranging from 80% among individuals aged 65–74 years to 89% among those  
165 aged 95 years and older. Table 3 shows the proportion of older adults with a high fraction of  
166 time with polypharmacy, i.e. exposed to polypharmacy for  $\geq 80\%$  of follow-up. In the total  
167 study population, 79.9% of older adults had a high fraction of time with polypharmacy,  
168 compared with 23.6% among persons with a new polypharmacy episode at baseline. After  
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  
171 probability 93% vs 78%,  $p < 0.01$ ). The proportion of nursing home residents with a high  
172 fraction of time with polypharmacy was higher than among community dwellers (90.7% vs  
173 79.1%). However, after adjustment for other covariates, this association was reversed  
174 (predicted probability 76.7% vs. 80.1%). In post-hoc analysis, we explored the interaction  
175 between living arrangement and drug dispensing scheme. This showed that community-  
176 dwellers with multi-dose dispensing were in fact more likely to have a high fraction of time  
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  
179 which yielded similar numbers, and using a cut-off value of  $\geq 50\%$  which left the association  
180 with other covariates largely unaffected although a larger proportion of older adults were  
181 classified as chronic polypharmacy users (Table S4 and S5).



## 183 **Discussion**

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

187 First, when focusing on the *duration* of polypharmacy episodes, our data clearly show that  
188 polypharmacy is persistent for a majority of older adults. About 75% of the individuals with  
189 polypharmacy at baseline remained exposed to polypharmacy for at least 12 consecutive  
190 months. Moreover, even though persons with a new polypharmacy episode at baseline were  
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  
196 true among those who are prescribed 3 to 4 medications for the management of chronic  
197 diseases (and who are likely to fluctuate around the threshold of 5 drugs used to define  
198 polypharmacy).

199 Another way to assess the longitudinal exposure to polypharmacy is to investigate the  
200 proportion of months that older adults spend with polypharmacy. Contrary to *duration*, which  
201 measures the length of continuous and uninterrupted polypharmacy episodes and is therefore  
202 particularly sensitive to grace periods and right censoring (e.g. survival), the *fraction of time*  
203 *with polypharmacy* describes the burden of polypharmacy with respect to the available  
204 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  
206 individuals exposed to polypharmacy at least 6 out of 12 months.<sup>32</sup> In the present study, we  
207 found that 80% of older adults had a high *fraction of time with polypharmacy* (i.e. spent  
208  $\geq 80\%$  of follow-up with polypharmacy), which is indicative of a chronic exposure. Risk  
209 factors associated with high fraction of time with polypharmacy included higher age, female  
210 gender, living in institution, chronic multimorbidity, and multi-dose dispensing<sup>33–35</sup>. When  
211 using the same cut-off value as Franchi et al.<sup>32</sup> – namely being exposed to polypharmacy  
212 during more than 50% of the available months – 42% of older adults who started a new  
213 polypharmacy episode at baseline had chronic polypharmacy in our study. An unexpected  
214 finding was that the adjusted probability of spending a large proportion of months with  
215 polypharmacy was higher among people residing in the community than in nursing homes.  
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  
218 dispensing had the largest fraction of time with polypharmacy. The finding that people with  
219 multi-dose dispensing spend a higher fraction of time with polypharmacy is in agreement  
220 with previous Swedish studies showing that persons with multi-dose dispensing have fewer  
221 changes made to their drug regimens (e.g. dose adjustments, drug discontinuations and newly  
222 prescribed drugs)<sup>30,36</sup>. One suggested reason for the fewer changes is that prescribers have the  
223 possibility to renew all drugs at once, which is not possible with ordinary prescriptions<sup>36</sup>.

224 There currently exists no consensual definition of polypharmacy, but two aspects have been  
225 widely discussed: the number of drugs that defines polypharmacy in a clinically meaningful  
226 way,<sup>37,38</sup> and the criteria that would allow for drawing the line between appropriate and  
227 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  
229 between chronic and transient polypharmacy.<sup>19</sup> Our study shows that exposure to  
230 polypharmacy is not always stable over time, and that transient polypharmacy episodes are  
231 not uncommon. The notion of *temporality* should thus be better accounted for in the future.  
232 Observational studies that have investigated the association between polypharmacy and  
233 negative health outcomes have seldom considered polypharmacy as a time-varying  
234 exposure.<sup>2,39</sup> Yet, doing so would considerably improve the assessment of harms of  
235 polypharmacy and could potentially elucidate the question whether the effect of  
236 polypharmacy is cumulative (i.e. longer exposure to polypharmacy leads to an accumulated  
237 risk of adverse effects) or if polypharmacy is hazardous even if exposure is short-lasting. The  
238 potential cumulative hazard of polypharmacy was recently highlighted in a British study,  
239 which demonstrated that the associations between polypharmacy and physical and cognitive  
240 capabilities was more pronounced among older adults with a long-term exposure to  
241 polypharmacy.<sup>23</sup>

#### 242 ***Strengths and limitations***

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



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

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

282

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286 **Conflict of Interest:** Authors have no conflicts of interest to report.

287 **Author Contributions:** All authors contributed to the study design, interpretation of  
288 findings, writing and review of the manuscript. Jonas W Wastesson and Lucas Morin  
289 performed analyses.

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291 collections, analysis and preparation of paper.

292

Elements of Financial/Personal Conflicts	*Author 1		Author 2		Author 3		Author 4	
	JWW		LM		MLL		KJ	
	Yes	No	Yes	No	Yes	No	Yes	No
<b>Employment or Affiliation</b>		X		X		X		X
<b>Grants/Funds</b>		X		X		X		X
<b>Honoraria</b>		X		X		X		X
<b>Speaker Forum</b>		X		X		X		X
<b>Consultant</b>		X		X		X		X
<b>Stocks</b>		X		X		X		X
<b>Royalties</b>		X		X		X		X
<b>Expert Testimony</b>		X		X		X		X
<b>Board Member</b>		X		X		X		X
<b>Patents</b>		X		X		X		X
<b>Personal Relationship</b>		X		X		X		X

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313 **Supplementary material**

314 Brief title: Supplementary analyses of chronicity of polypharmacy

315

313 **Figure captions**

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

327

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

332

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

<b>Sex, No (%)</b>	
Men	291,175 (40.9%)
Women	420,257 (59.1%)
<b>Age</b>	
Mean (SD)	77.4 (7.8)
<b>No (%)</b>	
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%)
<b>Living arrangement, No (%)</b>	
Community	658,693 (92.6%)
Institution	52,739 (7.4%)
<b>Number of chronic conditions</b>	
Mean (SD)	3.7 (2.6)
<b>No (%)</b>	
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%)
<b>Drug dispensing scheme, No (%)</b>	
Ordinary prescription	611,123 (85.9%)
Multi-dose dispensing	100,309 (14.1%)
<b>Number of drugs at baseline</b>	
Mean (SD)	8.0 (3.1)
<b>No (%)</b>	
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%)
≥10	178,446 (25.1%)
<b>Polypharmacy during the 6-month period before baseline, No (%)</b>	
No	21,361 (3.0%)
Yes	690,071 (97.0%)
<b>Death during follow-up, No (%)</b>	

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%)

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

	<b>Entire cohort (n=711,432 )</b>		<b>Older adults with a new polypharmacy episode at baseline (n=21,361)</b>	
	$\geq 6$ months	$\geq 12$ months	$\geq 6$ months	$\geq 12$ months
	%	%	%	%
<b>Total</b>	82.3	74.3	29.8	18.6
<b>Sex</b>				
Men	81.8	73.2	31.9	19.9
Women	82.7	75.0	28.2	17.6
<b>Age</b>				
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
<b>Living arrangement</b>				
Community	81.4	73.0	29.4	18.1
Institution	93.7	90.5	48.4	37.9
<b>Number of chronic conditions</b>				
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
$\geq 5$	91.7	86.7	44.1	31.5
<b>Drug dispensing scheme</b>				
Ordinary prescription	80.2	71.2	29.1	17.8
Multi-dose dispensing	95.5	93.0	51.4	41.8
<b>Number of drugs at baseline</b>				
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
$\geq 10$	97.8	95.5	78.4	67.3
<b>Death during follow-up</b>				
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

<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 ( $\geq 80\%$ ) during follow-up

	Entire cohort (n=711,432)			Older adults with a new polypharmacy episode at baseline (n=21,361)		
	Crude %	Adjusted % <sup>a</sup>	95% CI	Crude %	Adjusted % <sup>a</sup>	95% CI
<b>Total</b>	79.9	79.9	(79.8-80.0)	23.6	23.6	(23.1-24.2)
<b>Sex</b>						
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)
<b>Age</b>						
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)
<b>Living arrangement</b>						
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)
<b>Number of chronic conditions</b>						
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)
$\geq 5$	90.5	84.1	(83.9-84.3)	37.5	31.8	(29.8-33.8)
<b>Drug dispensing scheme</b>						
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)
<b>Number of drugs at baseline</b>						
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)
$\geq 10$	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.