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Assessing polypharmacy in the older population: Comparison of a self-reported and prescription based method

Johan Van der Heyden[1] | Finaba Berete[1,2] | Françoise Renard[1] | Johan Vanoverloop[3] | Brecht Devleesschauwer[1,4] | Karin De Ridder[1] | Olivier Bruyère[5]

[1]Department of Epidemiology and Public Health, Sciensano, Brussels, Belgium

[2]Department of Public Health, Epidemiology and Health Economics, University of Liège, Liège, Belgium

[3]Intermutualistic Agency (IMA-AIM), Brussels, Belgium

[4]Department of Veterinary Public Health and Food Safety, Ghent University, Merelbeke, Belgium

[5]WHO Collaborating Centre for Public Health Aspects of Musculoskeletal Health and Ageing, Department of Public Health, Epidemiology and Health Economics, University of Liege, Liège, Belgium

Correspondence
Johan Van der Heyden, Sciensano, Juliette Wytsmanstraat 14, 1050 Brussels, Belgium.
Email: johan.vanderheyden@sciensano.be

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Abstract

Purpose: To explore differences in the prevalence and determinants of polypharmacy in the older general population in Belgium between self-reported and prescription based estimates and assess the relative merits of each data source.

Methods: Data were used from participants aged ≥65 years of the Belgian national health survey 2013 ($n = 1950$). Detailed information was asked on the use of medicines in the past 24 h and linked with prescription data from the Belgian compulsory health insurance (BCHI). Agreement between polypharmacy (use or prescription ≥5 medicines) and excessive polypharmacy (≥10 medicines) between both sources was assessed with kappa statistics. Multinomial logistic regression was used to study determinants of moderate (5–9 medicines) and excessive polypharmacy (≥10 medicines) and over- and underestimation of prescription based compared to self-reported polypharmacy.

Results: Self-reported and prescription based polypharmacy prevalence estimates were respectively 27% and 32%. Overall agreement was moderate, but better in men (kappa 0.60) than in women (0.45). Determinants of moderate polypharmacy did not vary substantially by source of outcome indicator, but restrictions in activities of daily living (ADL), living in an institution and a history of a hospital admission was associated with self-reported based excessive polypharmacy only.

Conclusions: Surveys and prescription data measure polypharmacy from a different perspective, but overall conclusions in terms of prevalence and determinants of polypharmacy do not differ substantially by data source. Linking survey data with prescription data can combine the strengths of both data sources resulting in a better tool to explore polypharmacy at population level.

KEYWORDS
ageing, health survey, linkage, polypharmacy, population-based, prescription data

KEY POINTS

- The prevalence of self-reported and prescription based polypharmacy (simultaneous use or prescription ≥5 medicines) in the Belgian population ≥65 years is respectively 27% and 32%.
- There is a moderate agreement between the estimates from both sources, which is higher in men (kappa 0.60) than in women (kappa 0.45).

- Moderate polypharmacy is significantly associated with multimorbidity, an inpatient hospitalization in the past year and a higher number of contacts with the GP; excessive polypharmacy with lower secondary education, living in a nursing home, moderate and severe restrictions in activities of daily living and inpatient hospitalization in the past year.
- Health surveys in which detailed information is gathered on the use of medicines and prescription databases are complementary tools to study polypharmacy at population level.
- Linkages of survey data and prescription data offer new opportunities for research in the domain of polypharmacy.

1 | BACKGROUND

The ageing of the population has led to an increase of multimorbidity in many countries.[1–5] From a systematic review of the literature it appears that the prevalence of multimorbidity in older persons ranges from 55% to 98%.[6] For most chronic conditions there are disease-specific guidelines, including recommendations for the use of medicines to treat the disease or prevent complications. However, most clinical practice guidelines do not modify or discuss the applicability of their recommendations for older patients with multiple diseases and this inevitably leads to polypharmacy.[7,8] Polypharmacy can be appropriate, but is problematic when the increased risk of harm mainly due to drug–drug interactions and side effects outweighs plausible benefits.[9]

Obtaining a clear and comprehensive picture of polypharmacy is a big challenge. Studies on polypharmacy vary with regard to the definition, but also by setting, reference period, age group of the study population, type, volume and regularity of use of medicines considered. Regarding definition, there are two approaches. A first one takes into account the quality of prescribing,[10] but distinguishing appropriate and inappropriate polypharmacy remains difficult. A second approach advocates a definition based on the number of medications, but there is no theoretical basis that may confirm the number of medications required for such a definition.[11] A systematic review of numerical only definitions of polypharmacy found thresholds between ≥2 and ≥11, but the most commonly used approach is to define polypharmacy as the simultaneous use of 5 or more medicines on 1 day[10] and define excessive polypharmacy as the simultaneous use of 10 or more medicines.

Most population based studies on the use of medication are based on prescription data or self-reported survey data.[12] Prescription data might be more accurate as they are not prone to poor recall, but may not represent actual use. Often they are collected for reimbursement purposes and information on non-reimbursed medicines is lacking. Self-reported data (via a self-completed questionnaire, telephone interview, or face-to-face interview) provide information on the use of both prescribed and non-prescribed medicines. This can be supplemented by a medication inventory, whereby all medication packages are presented to interviewers, reducing any recall problems, as for instance is done in the National Health and Nutrition Examination Survey (NHANES), the Canadian Health Measures Survey (CHMS),[13] and the Belgian Health Interview Survey (BHIS).[14]

Comparison between prescription and self-reported data is essential for improved understanding of the relative merits of each source and the extent of potential misclassification of medication use in pharmacoepidemiological studies. It also adds evidence on the reliability of epidemiologic studies that quantify medication use through self-report, which is often the easiest way to gather this type of information. The comparison of information on polypharmacy of prescription based and self-reported data is useful to understand strengths and weaknesses of both data sources and gain further insights on how to better interpret results from those data sources.

In this study, data linkage is used to compare simultaneous polypharmacy on a single day based on prescription data from the Belgian compulsory health insurance (BCHI) with a similar indicator based on the number of prescribed and non-prescribed medicines used in the past 24 h according to the BHIS. The specific objectives of the study are (1) to assess to which extent polypharmacy and excessive polypharmacy are under- or overestimated if based on prescription data compared to reported use of medicines; (2) to explore differences and similarities in the estimates on the use of specific groups of medicines between prescription based and self-reported information; and (3) to investigate to which extent determinants of polypharmacy and excessive pharmacy in the older general population differ depending on the data source that was used to assess this.

2 | METHODS

2.1 | Data

The BHIS is household survey organized every 4 to 5 years. Participants are selected through a stratified clustered multistage sampling design.[15] The target population consists of all Belgian residents, including older people who live in nursing homes. In the BHIS, information is collected on the health status, health behavior, health care consumption and sociodemographic characteristics of all participants. As part of the Computer-Assisted Personal Interview (CAPI) respondents are asked to show to the interviewer the medicines they have used in the past 24 h. The interviewer records the brand name of the medicine and if available the national code which can be found on the package. For each medicine it is asked whether it was taken on doctor's prescription or not and what was the reason to take the

medicine. In a later stage information on the WHO Anatomical Therapeutic Chemical Classification (ATC) code and the reimbursement status is added by merging the data with information from the National Institute of Health and Disability Insurance.

BCHI data included comprehensive information on all reimbursed medicines for the years 2012, 2013 and 2014, more specifically: anonymized patient ID, date of prescription, national code of the medicine (with a direct link to the brand name), ATC code, quantity per package (QPP) and number of daily defined doses (DDD) per prescription.

For this study data were used of the BHIS 2013 participants aged 65 years and over. The participation rate of this survey at household level was 57.1%. Previous research showed that in the BHIS the participation rate of people aged 65 years and over is similar as in the younger age groups.[16] For 1950 respondents (96.4% of the BHIS participants within this age group) data could be linked with prescription data on reimbursed medicines from the BCHI.

2.2 | Outcome indicators and potential determinants

Polypharmacy status for both methods was classified into three groups: non-polypharmacy (<5 medicines), moderate polypharmacy (5–9 medicines), and excessive polypharmacy (≥10 medicines). This classification has been used in the literature before.[17] Some analyses were also conducted on a binary polypharmacy indicator (≥5 medicines). Self-reported polypharmacy was defined taking into account all medicines included in the official Belgian compendium of medicines.[18] This is a comprehensive list of medicines available in Belgian public pharmacies, including both prescription medicines (reimbursed or not) and over-the-counter medicines (OTC). Herbal medicines, homeopathic medicines and most of the food supplements are not included in line with other studies.[14,19] Simultaneous polypharmacy on the date of the interview based on the BCHI data was calculated by the method proposed by Fincke et al.[20] This method makes use of the date of dispensing of the medicine, the QPP and the DDD to estimate if a medicine is "active" on a particular day, which means that the prescription is recent enough to assume that the person has been using this medicine on that day. In our study this method was applied to assess if a medicine was "active" on the day of the interview.

Prescription data did not take into account non-reimbursed prescription medicines and OTC, because such information is not available in the BCHI database.

BHIS based potential determinants of polypharmacy status that were considered were gender, age, educational attainment, living situation, region of residence, multimorbidity, restrictions in activities of daily living (ADL), inpatient and day patient hospitalization in the past year and number of contacts with the general practitioner and the specialist in the past 2 months. Multimorbidity was defined as having suffered in the past year from at least two of the following diseases: serious heart disease, hypertension, obstructive lung disease, cancer, arthrosis or arthritis and diabetes. A similar survey-based multimorbidity indicator has been used in a Canadian study.[21] The ADL indicator in this study was based on questions on getting in and out of a bed or chair, dressing and undressing, bathing or showering, feeding yourself and using toilets from the European Health Interview Survey.[22]

2.3 | Statistical analyses

Agreement between self-reported and prescription based polypharmacy was assessed after having excluded important groups of medicines (in terms of use) which are always or usually OTC and/or

TABLE 1 Description of the sample

	N	Crude percentage (sample)	Weighted percentage (population)
Gender			
Men	858	44.0	42.3
Women	1092	56.0	57.7
Age			
65–74 years	998	51.2	50.1
75–84 years	714	36.6	37.5
85+ years	238	12.2	12.4
Education			
No diploma/ primary	491	25.2	27.8
Lower secondary	391	20.1	20.3
Higher secondary	499	25.6	26.6
Tertiary	543	27.9	25.3
No info	26	1.3	
Living situation			
Alone	644	33.0	32.9
At home with others	1203	61.7	63.1
Institution	84	4.3	4.0
Missing	19	1.0	
Region			
Flanders	731	37.5	61.3
Brussels	400	20.5	7.7
Wallonia	819	42.0	31.0
Multimorbidity			
Yes	683	35.0	35.9
No	1263	64.8	64.1
No info	4	0.2	
Restrictions in ADL[a]			
Severe	291	14.9	16.0
Moderate	256	13.1	12.2
None	1402	71.9	71.7
No info	1	0.1	

[a]Activities of daily living.

TABLE 2 Percentage of people aged 65 years and older with polypharmacy[a] and excessive polypharmacy[b] according to both sources and agreement[c] between both sources taking self-reported based data as reference

Polypharmacy[a]	Self-reported based[d]		Prescription based[e]		Sensitivity		Specificity		PPV[f]		NPV[g]		Kappa[c]		*n*
	%	95% CI	%	95% CI	%	95% CI	%	95% CI	%	95% CI	%	95% CI		95%CI	
Men - 65-74 years	22.2	(17.5–26.9)	27.9	(22.7–33.1)	85.7	(77.2–94.3)	87.0	(82.7–91.4)	62.6	(52.0–73.2)	96.0	(93.5–98.5)	0.64	0.56–0.72	469
Men - 75-84 years	29.0	(23.0–35.1)	35.7	(28.7–42.7)	78.2	(68.2–88.2)	81.3	(73.6–88.9)	60.3	(47.3–73.4)	91.1	(86.7–95.6)	0.54	0.44–0.65	314
Men - 85 years +	34.3	(19.6–48.9)	44.2	(28.5–59.9)	82.7	(64.1–100.0)	80.9	(64.1–97.8)	67.8	(41.1–94.6)	90.6	(80.7–100.0)	0.60	0.41–0.79	75
Men - all	25.7	(22.0–29.3)	32.1	(28.0–36.2)	82.4	(76.3–88.4)	84.6	(80.7–88.5)	62.3	(54.4–70.1)	93.9	(91.7–96.2)	0.60	0.54–0.66	858
Women - 65-74 years	24.0	(18.5–29.5)	27.8	(21.6–34.1)	70.8	(57.5–84.1)	85.1	(78.7–91.5)	54.5	(39.6–69.4)	92.0	(88.0–96.1)	0.50	0.42–0.59	529
Women - 75-84 years	31.7	(25.2–38.2)	34.8	(28.2–41.3)	66.2	(51.9–80.6)	80.1	(74.2–86.1)	55.4	(43.8–66.9)	86.5	(79.8–93.1)	0.44	0.35–0.53	400
Women - 85 years +	35.0	(25.9–44.0)	41.1	(31.4–50.8)	64.9	(47.9–81.9)	72.8	(61.5–84.2)	49.3	(32.2–66.4)	83.6	(74.8–92.4)	0.34	0.20–0.49	163
Women - all	28.6	(24.8–32.5)	32.6	(28.5–36.7)	67.7	(52.4–68.3)	81.5	(77.4–85.6)	53.9	(48.6–65.0)	88.8	(85.4–92.2)	0.45	0.40–0.47	1092
All	27.4	(24.6–30.2)	32.4	(29.4–35.3)	73.8	(68.3–79.4)	82.8	(79.8–85.8)	57.5	(51.5–63.5)	91.0	(88.7–93.2)	0.52	0.47–0.56	1950
Excessive polypharmacy[b]															
Men - 65-74 years	2.4	(0.8–4.1)	2.8	(1.2–4.5)	60.4	(4.3–100.0)	98.4	(97.1–99.6)	39.1	(5.9–72.2)	99.3	(98.2–100.0)	0.46	(0.19–0.74)	469
Men - 75-84 years	5.4	(2.6–8.3)	4.0	(1.4–6.6)	45.5	(10.8–80.3)	98.2	(96.3–100.0)	51.5	(10.2–92.8)	97.7	(95.8–99.6)	0.46	(0.20–0.72)	314
Men - 85 years +	9.0	(0.0–20.0)	1.2	(0.0–3.5)	32.4	(0.0–100.0)	100.0	-	100.0	-	97.5	(94.1–100.0)	0.48	(0.00–1.00)	75
Men – all	4.1	(2.4–5.8)	3.1	(1.8–4.4)	49.1	(24.3–73.9)	98.5	(97.5–99.4)	46.9	(23.1–70.7)	98.6	(97.6–99.5)	0.47	(0.28–0.65)	858
Women - 65-74 years	4.8	(1.1–8.5)	1.5	(0.2–2.8)	2.4	(0.0–8.5)	99.0	(98.1–99.9)	8.5	(0.0–28.9)	96.4	(92.8–100.0)	0.02	(0.00–0.13)	529
Women - 75-84 years	2.0	(0.6–3.3)	2.4	(0.9–3.9)	6.7	(0.0–25.2)	98.5	(97.4–99.6)	4.2	(0.0–14.3)	99.1	(98.2–100.0)	0.04	(0.00–0.22)	400
Women - 85 years +	3.4	(0.8–6.0)	1.2	(0.0–2.9)	36.0	(0.0–100.0)	100.0	-	100.0	-	98.8	(97.3–100.0)	0.53	(0.00–1.00)	163
Women – all	3.5	(1.7–5.3)	1.8	(1.0–2.7)	7.1	(0.0–18.0)	98.9	(98.3–99.5)	13.9	(0.0–32.5)	97.8	(96.1–99.5)	0.08	(0.00–0.21)	1092
All	3.7	(2.5–5.0)	2.4	(1.6–3.1)	26.3	(9.7–42.8)	98.7	(98.2–99.3)	34.8	(17.9–51.7)	98.1	(97.0–99.2)	0.28	(0.16–0.41)	1950

[a]≥5 medicines.
[b]≥10 medicines.
[c]For the calculation of agreement measures important ATC groups which are always or usually OTC and/or not reimbursed were excluded from both data sources (G04CA, N02BE, N05CF, N05BA, N05CD, A12AX, M05BA).
[d]Not reimbursed prescription medicines and OTC (over-the-counter medicines) included.
[e]Not reimbursed prescription medicines and OTC not included.
[f]Positive predictive value.
[g]Negative predictive value.

TABLE 3 Reported use of medicines in the past 24 h versus recent prescription, by ATC4 code for the 25 most used and prescribed medicines, men aged 65 years and older

		Reported use of a medicine in this category in past 24 h (E1)		Recent prescription of a medicine in this category in BCHI[a] data (E2)		Absolute difference between both estimates (E2)–(E1)*		Agreement between both estimates	
ATC4	Category	%	95%CI	%	95%CI	%	95%CI	kappa	95%CI
C10AA	Hydroxymethylglutaryl CoA reductase inhibitors (statins)	33.6	(29.3;37.8)	39.3	(34.9;43.7)	5.7	(−0.3;11.7)	0.63	(0.58–0.69)
B01AC	Platelet aggregation inhibitors excl. heparin	29.0	(25.2;32.9)	31.8	(27.7;35.8)	2.8	(−2.8;8.4)	0.61	(0.55–0.67)
C07AB	Beta blocking agents. selective	19.8	(16.4;23.3)	19.5	(15.9–23.1)	−0.3	(−5.3;4.6)	0.63	(0.56–0.69)
A02BC	Proton pump inhibitors	17.3	(13.7;20.8)	22.7	(18.6;26.7)	5.4*	(0.0;10.7)	0.69	(0.63–0.76)
C09AA	Angiotensin-converting enzyme inhibitors. plain	12.1	(9.3:15.0)	17.0	(13.8;20.3)	4.9*	(0.6;9.2))	0.72	(0.65–0.79)
C08CA	Dihydropyridine derivatives	10.5	(7.7:13.2)	14.9	(11.8;18.0)	4.4*	(0.3;8.6)	0.77	(0.71;0.84)
A10BA	Biguanides	8.9	(6.7:11.5)	8.8	(6.7;10.9)	−0.1	(−3.2;3.0)	0.63	(0.53–0.72)
G04CA	Alpha-adrenoreceptor antagonists	8.5	(6.0:10.9)	Not listed because only partial information in prescription database					
M04AA	Preparations inhibiting uric acid production	7.5	(5.4:9.6)	7.6	(5.3;9.9)	0.1	(−3.1:3.2)	0.64	(0.54;0.74)
N05BA	Benzodiazepine derivatives	7.0	(5.0:8.9)	Not listed because no information in prescription database					
C03CA	Sulfonamides, plain	5.6	(3.6:7.6)	6.5	(4.6:8.4)	0.9	(−1.9:3.7)	0.66	(0.55;0.77)
C09CA	Angiotensin II receptor blockers, plain	5.6	(3.6:7.6)	8.5	(6.1;11.0)	2.9	(−0.2:6.1)	0.74	(0.65;0.83)
C09DA	Angiotensin II receptor blockers and diuretics	4.9	(3.0:6.9)	5.8	(3.8;7.9)	0.9	(−1.9:3.7)	0.78	(0.68;0.88)
A10BB	Sulfonylureas	4.8	(3.1:6.5)	6.1	(4.0:8.1))	1.2	(−1.4:3.9)	0.78	(0.69;0.88)
B01AA	Vitamin K antagonists	4.2	(2.5:5.8)	4.5	(2.6;6.4)	0.3	(−2.2:2.9)	0.69	(0.56;0.81)
R03AK	Adrenergics in combination with corticosteroids or other drugs	4.0	(2.2:5.8)	4.7	(3.1;6.4)	0.8	(−1.7:3.2)	0.55	(0.41;0.69)
N06AX	Antidepressants	3.8	(2.0:5.5)	3.8	(2.0;5.6)	0.0	(−2.5:2.5)	0.52	(0.37–0.68)
C07BB	Beta blocking agents, selective, and thiazides	3.6	(1.8:5.3)	3.1	(1.4;4.8)	−0.4	(−2.9:2.0)	0.86	(0.76;0.96)
C01DX	Vasodilators used in cardiac diseases	3.5	(2.1:4.9)	5.7	(3.6;7.7)	2.2	(−0.3:4.6)	0.72	(0.60;0.83)
N02BE	Anilides	3.4	(1.9:4.9)	Not listed because only partial information in prescription database					
N06AB	Selective serotonin reuptake inhibitors	3.1	(1.8:4.3)	4.3	(2.8;5.8)	1.2	(−0.7:3.2)	0.79	(0.68;0.90)
N05CD	Benzodiazepine derivatives	3.1	(1.7:4.5)	Not listed because no information in prescription database					
C07AA	Beta blocking agents, non-selective	3.0	(1.8:4.3)	3.5	(2.0;5.1)	0.5	(−1.5:2.5)	0.78	(0.66;0.91)
H03AA	Thyroid hormones	2.3	(1.3:3.3)	2.5	(1.4;3.6)	0.2	(−1.3:1.7)	0.66	(0.49;0.83)
R03BB	Anticholinergics	2.2	(1.1:3.4)	2.2	(0.9;3.5)	0.0	(−1.7:1.7)	0.61	(0.42;0.80)
C09BA	Angiotensin-converting enzyme inhibitors and diuretics	2.0	(0.9:3.1)	3.7	(1.7:4.4)	1.7	(−0.2:3.6)	0.57	(0.40;0.74)
R05CB	Mucolytics	1.7	(0.9:3.1)	5.6	(3.7;7.6)	4.0*	(1.8:6.2)	0.32	(0.17;0.48)
H02AB	Glucocorticoids	1.3	(0.7:2.4)	3.6	(1.8;5.4)	2.3*	(0.4:4.3)	0.24	(0.06;0.42)
R03AC	Selective beta-2-adrenoreceptor agonists	0.9	(0.1:1,6)	3.2	(1.4;5.0)	2.3*	(0.3:4.3)	0.38	(0.18;0.59)
S01ED	Beta blocking agents (ophthalmological treatment)	0.7	(0.1:1.2)	2.7	(1.1;4.4)	2.0*	(0.3:3.8)	0.22	(0.02;0.43)

[a]Belgian Compulsory Health Insurance.
*Significant difference ($p < 0.05$).

not reimbursed (ATC G04CA, N02BE, N05CF, N05BA, N05CD, A12AX, M05BA) from both data sources. Using the self-reported based estimates as reference we calculated the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV), with corresponding 95% confidence intervals, of prescription based polypharmacy (≥5 medicines) and excessive polypharmacy (≥10

TABLE 4 Reported use of medicines in the past 24 h versus recent prescription, by ATC4 code for the 25 most used and prescribed medicines[a], women aged 65 years and older

		Reported use of a medicine in this category in past 24 h (E1)		Recent prescription of a medicine in this category in BCHI[a] data (E2)		Absolute difference between both estimates (E2)–(E1)*		Agreement between both estimates	
ATC4	Category	%	95%CI	%	95%CI	%	95%CI	kappa	95%CI
C10AA	Hydroxymethylglutaryl CoA reductase inhibitors (statins)	30.8	(26.9;34.7)	39.3	(35.1;43.6)	8.5*	(2.7;14.3)	0.63	(0.58;0.68)
B01AC	Platelet aggregation inhibitors excl. heparin	20.4	(17.2:23.7)	25.7	(21.8;29.7)	5.3*	(0.2;10.4)	0.64	(0.59;0.70)
C07AB	Beta blocking agents. selective	17.9	(14.8:20.9)	17.3	(14.1;20.6)	−0.5	(−5.0;3.9)	0.56	(0.50;0.62)
A02BC	Proton pump inhibitors	15.5	(12.6:18.5)	24.4	(20.5;28.2)	8.8*	(4.0;13.6)	0.60	(0.54;0.66)
N05BA	Benzodiazepine derivatives	12.4	(10.0:14.8)	Not listed because no information in the prescription database					
H03AA	Thyroid hormones	11.5	(9.2:14.7)	11.9	(9.2;14.7)	0.4	(−3.2;4,1)	0.73	(0.67;0.80)
C09AA	Angiotensin-converting enzyme inhibitors. plain	9.1	(6.8:11.4)	14.8	(11.5–18.2)	5.7*	1.7;9.7)	0.65	(0.59;0.72)
A10BA	Biguanides	8.5	(5.9:11.0)	7.9	(5.3–10.4)	−0.6	(−4.2;3.0)	0.65	(0.57–0.73)
N06AB	Selective serotonin reuptake inhibitors	8.0	(5.5:10.5)	12.2	(9.4–15.1)	4.2	(0.5;8.0)	0.73	(0.66–0.79)
C08CA	Dihydropyridine derivatives	7.6	(5.7:9.6)	11.1	(8.7–13.5)	3.4	(0.3;6.5)	0.67	(0.60–0.75)
N05CD	Benzodiazepine derivatives	7.5	(5.1:9.8)	Not listed because no information in the prescription database					
N02BE	Anilides	7.3	(5.0:9.6)	Not listed because only partial information in the prescription database					
N06AX	Antidepressants	4.7	(3.1:6.2)	5.2	(3.5;6.8)	0.5	(−1.7;2.8)	0.71	(0.62–0.81)
C09DA	Angiotensin II receptor blockers and diuretics	5.4	(3.5:7.3)	5.8	(3.8–7.7)	0.3	(−2.4;3.1)	0.76	(0.68;0.85)
C09CA	Angiotensin II receptor blockers - plain	5.0	(3.0:7.0)	7.2	(5.0;9.4)	2.2	(−0.7;5.2)	0.74	(0.66–0.82)
C03EA	Low-ceiling diuretics and potassium-sparing agents	5.2	(3.3:7.1)	5.9	(4.0;7.7)	0.7	(−2.0;3;3)	0.66	(0.56–0.75)
C03CA	Sulfonamides. plain	5.0	(2.6:7.5)	5.9	(4.1;7.7)	0.8	(−2.2;3.8)	0.55	(0.44;0.66)
C07BB	Beta blocking agents. selective. and thiazides	4.5	(2.6:6.4)	5.1	(3.2;7.0)	0.6	(−2.1;3.3)	0.73	(0.64;0.83)
A12AX	Calcium. combinations with vitamin D and/or other drugs	4.6	(2.8:6.4)	Not listed because only partial information in the prescription database					
C07AA	Beta blocking agents. non-selective	4.1	(2.6:5.7)	4.3	(2.8;5.8)	0.2	(−2.0;2.3)	0.74	(0.64;0.84)
R03AK	Adrenergics in combination with corticosteroids or other drugs	4.2	(1.8:6.5)	5.2	(2.8;7.7)	1.1	(−2.3;4.5)	0.82	(0.73–0.90)
N05CF	Benzodiazepine related drugs	4.0	(2.4:5.6)	Not listed because no information in the prescription database					
N02AX	Opioids	3.1	(2.1:4.2)	1.6	(0.8;2.3)	−1.6*	(−2.8; −0.3)	0.44	(0.28;0.61)
C01DX	Vasodilators used in cardiac diseases	3.4	(1.5:5.3)	4.9	(2.8;7.0)	1.5	(−1.3;4.4)	0.81	(0.72;0.90)
C09BA	Angiotensin-converting enzyme inhibitors and diuretics	3.5	(1.9:5.1)	4.0	(2.3;5.6)	0.4	(−1.8;2.7)	0.73	(0.62;0.84)
N07CA	Antivertigo preparations	3.0	(1.8:4.2)	4.1	(2.6;5.6)	1.1	(−0.8;3,1)	0.73	(0.62;0.84)
S01ED	Beta blocking agents	1.9	(0.6:3.2)	3.9	(2.4;5.3)	2.0*	(0.0;4;0)	0.39	(0.23;0.54)
R05CB	Mucolytics	1.8	0.9;5.6)	4.5	(3.0;6.0)	2.7*	(1.0:4.5)	0.42	(0.27;0.57)
M05BA	Bisphosphonates	1.3	(0.5:2.1)	4.8	(3.2;6.4)	3.5*	(1.7:5.3)	0.27	(0.13;0.41)
R06AE	Piperazine derivatives	1.3	(0.5:2.1)	3.9	(1.6;6.2)	2.6*	(0.1:5.0)	0.39	(0.23;0.55)
M05BB	Bisphosphonates. combinations	0.9	(0.3:1.4)	3.8	(2.3;5.4)	3.0*	(1.3:4.6)	0.31	(0.15;0.48)

[a]Belgian Compulsory Health Insurance.

*Significant difference ($p < 0.05$).

medicines). The agreement between the estimates from both sources was assessed with kappa statistics, including 95% confidence intervals.

To gain further insights comparisons were also made between prevalence estimates of self-reported use and recent prescription of specific types of medicines at the ATC 4th level (ATC4), which corresponds in the ATC classification system with the chemical subgroup. This was done for the 25 ATC4 group categories that were most frequently reported and prescribed. These represent more than 70% of the total daily number of consumed and prescribed medicines, both in men and women.

For all groups of medicines, except the ATC groups mentioned above, statistically significant differences were assessed with the delta method.[23] In addition the agreement of both estimates was assessed with kappa statistics, including 95% confidence intervals.

In a subsequent step potential determinants of moderate and excessive polypharmacy were explored via odds ratios (OR) of multinomial logistic regression models. This was first done separately for prescription and self-reported based estimates. Then multinomial models were fitted to investigate potential determinants of under- and overestimation of the prescription versus the self-reported based estimate.

TABLE 5 Determinants of moderate (5–9 medicines) and excessive polypharmacy (≥10 medicines) in the population aged 65 years and older. Results from multinomial logit models

	Self-reported based estimates[a]		Prescription based estimates[b]	
	Moderate polypharmacy OR[c] (+95% CI)	Excessive polypharmacy OR[c] (+95% CI)	Moderate polypharmacy OR[c] (+95% CI)	Excessive polypharmacy OR[c] (+95% CI)
Female	0.97 (0.72–1.31)	0.73 (0.32–1.66)	0.86 (0.63–1.16)	0.49 (0.21–1.17)
Age				
65–74 years	Ref	Ref	Ref	Ref
75–84 years	1.29 (0.91–1.82)	0.61 (0.28–1.32)	1.27 (0.91–1.76)	1.17 (0.54–2.55)
85+ years	1.04 (0.61–1.77)	0.45 (0.12–1.68)	1.54 (0.95–2.50)	0.43 (0.14–1.35)
Education				
No diploma/primary	0.96 (0.59–1.55)	0.97 (0.39–2.37)	1.09 (0.69–1.73)	0.74 (0.29–1.91)
Lower secondary	1.51 (0.94–2.41)	3.11 (1.01–9.60)*	1.19 (0.77–1.84)	2.03 (0.78–5.30)
Higher secondary	0.80 (0.51–1.26)	0.84 (0.32–2.21)	1.13 (0.75–1.73)	1.61 (0.59–4.41)
Tertiary	Ref	Ref	Ref	Ref
Living situation				
At home with others	Ref	Ref	Ref	Ref
At home alone	1.30 (0.91–1.88)	0.53 (0.22–1.31)	1.12 (0.80–1.57)	1.06 (0.44–2.57)
In a nursing home	1.49 (0.70–3.17)	3.94 (1.14–13.60)*	1.15 (0.51–2.59)	1.71 (0.39–7.43)
Region				
Flanders	Ref	Ref	Ref	Ref
Brussels	1.18 (0.80–1.74)	0.91 (0.39–2.11)	0.97 (0.67–1.41)	1.67 (0.64–4.33)
Wallonia	1.12 (0.80–1.57)	1.14 (0.61–2.11)	0.95 (0.70–1.30)	2.01 (0.96–4.24)
Multimorbidity	3.58 (2.60–4.94)[a]	4.42 (2.09–9.35)*	3.93 (2.83–5.44)*	7.35 (3.25–16.65)*
Restrictions in ADL[d]				
No restrictions	Ref	Ref	Ref	Ref
Moderate restrictions	1.30 (0.84–2.04)	3.47 (1.31–9.18)*	1.08 (0.70–1.69)	1.65 (0.64–4.23)
Severe restrictions	1.61 (0.98–2.65)	4.74 (1.59–14.09)*	1.01 (0.63–1.61)	2.37 (0.93–6.05)
Inpatient hospitalization <1 year	1.63 (1.12–2.37)*	3.47 (1.35–8.92)*	1.87 (1.27–2.75)*	1.78 (0.84–3.80)
Day patient hospitalization <1 year	1.06 (0.67–1.69)	0.52 (0.17–1.59)	0.78 (0.50–1.21)	0.34 (0.11–1.06)
Number contacts general practitioner <2 months	1.22 (1.04–1.42)*	1.18 (1.01–1.38)*	1.27 (1.09–1.50)*	1.30 (1.08–1.57)*
Number contacts specialist <2 months	1.00 (0.94–1.07)	1.04 (0.95–1.14)	1.04 (0.95–1.14)	1.07 (0.96–1.20)

[a]Not reimbursed prescription medicines and OTC (over-the-counter medicines) included.
[b]Not reimbursed prescription medicines and OTC not included.
[c]Odds ratio.
[d]Activities of daily living.
*Significant difference ($p < 0.05$).

TABLE 6 Determinants of under- and overestimation of prescription based polypharmacy status[a] in the population aged 65 years and older (reference = self-reported based estimate[b]). Results from multinomial logit models

	Underestimation[c] OR[e] (+95% CI)	Overestimation[d] OR[e] (+95% CI)
Female	1.56 (1.01–2.41)*	1.19 (0.79–1.78)
Age		
64–74 years	Ref	Ref
75–84 years	0.98 (0.60–1.61)	1.18 (0.77–1.81)
85+ years	0.74 (0.33–1.66)	1.39 (0.74–2.61)
Education		
No diploma/primary	1.84 (1.03–3.29)*	1.94 (1.08–3.51)*
Lower secondary	2.74 (1.41–5.35)*	1.36 (0.77–2.41)
Higher secondary	1.32 (0.76–2.31)	2.21 (1.28–3.84)*
Tertiary	Ref	Ref
Living situation		
At home with others	Ref	Ref
At home alone	0.83 (0.48–1.43)	0.88 (0.56–1.38)
In a nursing home	2.00 (0.81–4.98)	1.07 (0.38–3.03)
Region		
Flanders	Ref	Ref
Brussels	1.44 (0.87–2.37)	1.23 (0.77–1.98)
Wallonia	1.29 (0.83–2.01)	1.17 (0.78–1.98)
Multimorbidity	2.10 (1.32–3.35)*	2.39 (1.55–3.68)*
Restrictions in ADL[e]		
No restrictions	Ref	Ref
Moderate restrictions	2.33 (1.37–3.96)*	1.22 (0.71–2.09)
Severe restrictions	1.65 (0.85–3.19)	0.69 (0,39-1,23)
Inpatient hospitalization <1 year	1.99 (1.15–3.43)*	1.50 (0.89–2.53)
Day patient hospitalization <1 year	0.88 (0.47–1.64)	0.70 (0.37–1.30)
Number contacts general practitioner <2 months	1.06 (0.96–1.16)	1.09 (1.00–1.19)*
Number contacts specialist <2 months	0.99 (0.88–1.11)	1.00 (0.93–1.07)

[a]Not reimbursed prescription medicines and OTC (over-the-counter medicines) not included.
[b]Not reimbursed prescription medicines and OTC included.
[c]Non-polypharmacy according to the prescription based definition and moderate/excessive polypharmacy according to the self-reported based definition OR moderate polypharmacy according to the prescription based definition and excessive polypharmacy according to the self-reported based definition.
[d]Excessive polypharmacy according to the prescription based definition and non-polypharmacy/moderate polypharmacy according to the self-reported based definition OR moderate/excessive polypharmacy according to the prescription based definition and non-polypharmacy according to the self-reported based definition.
[e]Odds ratio.
[f]Activities of daily living.
*Significant difference ($p < 0.05$).

Analyses were conducted with SAS 9.4. and Stata 16.0 taking into account the design settings of the BHIS, including the survey weights, household clusters, and strata.

3 | RESULTS

Table 1 provides information on the distribution of the study sample by socio-demographic and health characteristics, before and after the application of survey weights.

The prescription based prevalence estimates of polypharmacy (≥5 medicines) and excessive polypharmacy (≥10 medicines) in the Belgian population aged 65 years and over are respectively 32.4% and 2.4%. Similar survey-based estimates based on the use of medicines are respectively 27.4% and 3.7% (Table 2). The match between self-reported and prescription based polypharmacy (≥5 medicines) is reasonable in men, with a sensitivity of 82.1%, a specificity of 84.6% and a kappa of 0.60. In women the agreement between self-reported and prescription based assessment of polypharmacy (≥5 medicines) is weaker (kappa 0.45). Table 2 further shows that there is a poor agreement between self-reported and prescription based excessive polypharmacy, which is again worse in women.

Tables 3 and 4 present prevalence estimates of the use in the past 24 h and a recent prescription for the 25 most frequently reported and prescribed ATC4 categories for which information is available in both databases.

Overall there is a good agreement between self-reported and prescription based estimates, with most kappas being higher than 0.50. For most ATC4 categories higher prevalence estimates are obtained for a recent prescription than for use in the past 24 h.

Results from the multinomial logistic regression analyses (Table 5) show that regardless of the source of the data used, moderate polypharmacy is significantly associated with multimorbidity, inpatient hospitalization in the past year and a higher number of contacts with the GP in the past 2 months.

There is a significant association between self-reported based excessive polypharmacy and lower secondary education, living in a nursing home, moderate and severe restrictions in ADL, and inpatient hospitalization in the past year. However, no such significant associations are found for prescription based excessive polypharmacy (Table 5).

Underestimation of polypharmacy status in older people (of prescription based compared to self-reported based estimates) occurs significantly more often in women, people with low education, multimorbidity, moderate restrictions in ADL and an inpatient hospitalization in the past year (Table 6). Overestimation of the polypharmacy status (of prescription based compared to self-reported based estimates) is significantly associated with multimorbidity and a higher number of contacts with the GP in the past 2 months.

4 | DISCUSSION

To our knowledge this is the first study that assessed polypharmacy within the same population based sample comparing self-reported

and prescription based estimates. Cautiousness is needed to interpret the results because the first data source also includes not reimbursed prescription medicines and OTC, whereas the second one reimbursed medicines only, but even when only comparable medication groups were considered, we found that overall agreement was moderate. Determinants of moderate polypharmacy and excessive polypharmacy did not vary substantially by source of outcome indicator. Differences in the classification of the polypharmacy status between the two sources were associated with education, health status and health care use.

In many countries there is a systematic collection of prescription data, often linked to the reimbursement of medicines. Many population based polypharmacy studies use such prescription data,[24–29] which are considered to be reliable. However, the value of prescription data to assess polypharmacy in the population depends on several factors, the most important ones being the completeness of the target population included in the database and the validity and degree of the completeness of the registered data.[30] An important disadvantage of most pharmacoepidemiological databases is the lack of information on OTC and prescription medicines not subsidized by the National Health Insurance. Furthermore, studies using prescription data do not take into account that due to non-compliance and the intermittent use of prescribed medicines in case of symptoms only (e.g. painkillers), prescription data will not always correctly reflect the actual use that causes the hazardous effects of polypharmacy, such as adverse drug reactions and drug–drug interactions.[31,32]

Surveys collect information on the actual use of medicines, and a number of studies have used this information to study polypharmacy.[33–36] Associations between polypharmacy and multimorbidity, functional limitations, educational attainment and visits to physicians, observed in our study, were also found in these studies. However, whereas most of these studies showed a higher likelihood of polypharmacy with increasing age and female gender, this was not observed in our study. In the BHIS interviewers did a visual inspection of the brand names of the medicines that were consumed and the reference period was short (24 h). For this reason and also because hazardous effects of polypharmacy are very much related to drug–drug interactions following the actual consumption of medicines, we used the self-reported data as reference for the comparison analyses. As both methods assess polypharmacy in a different way no perfect match was expected. The fact that the self-reported based estimate of polypharmacy is somewhat lower than the prescription based estimate may be related to an underreporting of medicines in the survey, but also to an overestimation of simultaneous polypharmacy in the prescription data, and this despite the fact that non reimbursed medicines and OTC medicines are not included in the latter database. Possible hypotheses for gender differences with respect to the agreement between self-reported and prescription based polypharmacy are gender differences in therapeutic compliance and in the use of medicines which were prescribed earlier, hence not identified in the insurance database as ‘‘active medicines.’’

To gain further insights into differences between reported use and recent prescription of particular groups of medicines, we compared this for the most commonly used ATC4 groups. Although a comparison at ATC5 group level (the chemical substance) is more relevant if the emphasis lies on the number of pills a patient takes and the problems/confusion that can go together with it, and a comparison at ATC3 group level (the therapeutic subgroup) more relevant if the emphasis lies on the interactions between different types of medication that can cause dizziness, confusion, delirium,.., we opted for the ATC4 group level (the chemical subgroup), because it was found that the simultaneous use of medicines belonging to the same therapeutic subgroup occurs regularly, whereas this is not the case for medicines of the same chemical subgroup, and our sample was too small to provide sufficiently accurate estimates of the use of medicines at the ATC5 group level. Our results were quite satisfactory, with moderate to good levels of agreement for most groups, which is compatible with other studies in which this was assessed.[12,37,38]

It is remarkable that the significant associations between the self-reported based indicator of excessive polypharmacy and restrictions in ADL, living in an institution and a history of a hospital admission were not significant when using the prescription based estimate as outcome indicator. Other studies have found associations between polypharmacy and these factors.[33,39–42] Furthermore, self-reported excessive polypharmacy estimates are higher than estimates based on self-reports, which is logical because also OTC and not reimbursed prescription medicines are considered. These findings suggest that the assessment of excessive polypharmacy is more accurate when it is based on self-reports.383.

Our results further indicate that differences in the classification of the polypharmacy status (no polypharmacy/moderate polypharmacy/excessive polypharmacy) between self-reported and prescription based estimates vary by population group. A lower education and the presence of multimorbidity are associated with more discrepancies in the polypharmacy status between both sources. A hypothesis is that the validity of self-reported information in these population groups is probably weaker as a result of more incomplete reporting of the medicines that have been used in the past 24 h by these groups. This needs to be taken into consideration when interpreting studies on determinants of polypharmacy based on survey data.

According to the self-reported information people in nursing homes and with restrictions in ADL have higher risk of excessive polypharmacy, but this association is not seen in the prescription data. This could be related to the fact that these people may have received more assistance form caregivers when completing the survey.

4.1 | Strengths and limitations of the study

Strengths of this study are that is population-based, it includes nursing home residents and information on self-reported and prescription based use of medicines was obtained from the same individuals. Limitations are mainly related to the validity of the information that is obtained. Even though the self-reported indicator is based on medicines that are actually shown to the interviewer, the list can be

incomplete due to reluctance of the respondent to disclose the use of particular medicines. Furthermore medicines could have been missed if they are not taken daily, but every other day. With respect to the prescription based indicator, Fincke's method to identify an active medicine on the date of the interview is a good approximation, but as the frequency and regularity of use and the dose per day is unknown, misclassification is possible.

Finally, in this study the definition of polypharmacy is based on the simple counting of medicines, without taking into account the reason and the regularity of the use/prescription, the specific medicines that are combined and the existing co-morbidity. Further population based studies on polypharmacy should focus on inappropriate polypharmacy and explore and compare data sources which are most suitable to investigate this.

5 | CONCLUSIONS

Both health surveys and prescription databases are useful instruments to assess polypharmacy in the general older population. In Belgium there is a reasonable agreement between the outcomes generated by both sources. Whereas determinants of moderate polypharmacy do not vary substantially by source of outcome indicator, self-reported based estimates seem to identify better than prescription based estimates in which population groups excessive polypharmacy occurs more often. From our study it is clear that each data source alone has advantages and limitations. Linkage of survey data, administrative databases and clinical databases will create opportunities to study polypharmacy at population level making use of more appropriate and relevant outcome indicators.

Linking survey data with prescription data can combine the strengths of both data sources resulting in a better tool to explore polypharmacy at population level.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ETHICS STATEMENT

This study was carried out using the individual linkage between the BHIS 2013 data and the BCHI data. The BHIS 2013 was carried out in line with the Belgian privacy legislation and has been approved by the ethics committee of the University hospital of Ghent, Belgium, on October, 1st 2012 (advice EC UZG 2012/658). The participation to BHIS is voluntary. No written consent was foreseen. Participation was equivalent to giving consent. In addition, for the data linkage, an authorization was obtained from the Belgian Information Security Committee (local reference: Deliberation No. 17/119 of December 19, 2017, amended on September 3, 2019).

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