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SHORT REPORT

Trends of polypharmacy among older people in Asia, Australia and the United Kingdom: a multinational population-based study

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Abstract

Background: Polypharmacy among older people represents a global challenge due to its association with adverse drug events. The reported prevalence of polypharmacy varies widely across countries, and is particularly high in Asian countries. However, there is no multinational study using standardised measurements exploring variations in prescribing trends.
Objective: To compare polypharmacy trends in older people in Asia, Australia and the United Kingdom.
Design: Multinational, retrospective, time-trend, observational study using a common study protocol.
Setting: Outpatient and community settings.
Subjects: All individuals aged ≥ 65 years between 2013 and 2016.
Methods: We defined polypharmacy as the concomitant use of ≥ 5 medications for ≥ 45 days per year. We estimated the annual prevalence of polypharmacy and calculated average annual percentage change (AAPC) to assess the time trends.
Results: A total of 1.62 million individuals were included in this study. The highest prevalence of polypharmacy was observed in Hong Kong (46.4%), followed by Taiwan (38.8%), South Korea (32.0%), the United Kingdom (23.5%) and Australia (20.1%) in 2016. For the time trend, the Asian region showed a steady increase, particularly in Hong Kong and South Korea (AAPC: Hong Kong, 2.7%; South Korea, 1.8%; Taiwan, 1.0%). However, Australia and the United Kingdom showed a

decreasing trend (Australia, −4.9%; the United Kingdom, −1.1%).

Conclusions: Polypharmacy prevalence in older people was higher in Hong Kong, Taiwan and South Korea, with an increasing trend over time, compared with Australia and the United Kingdom. Our findings underline the necessity to monitor polypharmacy among older people in Asia by conducting government-level interventions and introducing medicine-optimisation strategies.

Keywords: Polypharmacy, Older people, Multinational study, Drug utilisation

Key Points

- Polypharmacy prevalence in older people was higher in Hong Kong, Taiwan and South Korea compared with the United Kingdom and Australia.
- The Asian region showed a steady increase, particularly in Hong Kong (average annual percentage change: Hong Kong, 2.7%; South Korea, 1.8%; Taiwan, 1.0%).
- Australia (−4.9%) and the United Kingdom (−1.1%) showed a decreasing trend.
- Our findings underline the necessity to monitor polypharmacy among older people in Asia.

Introduction

Polypharmacy in older people has become a global challenge in recent years, especially with increased multimorbidity [1]. Older people are vulnerable to adverse drug events due to physiological changes associated with ageing (i.e. impairment of metabolism, drug excretion) [2], which could induce drug–drug or drug–disease interactions. Previous studies reported a substantial burden of adverse drug reactions across countries [3–6], and more than 2-fold risks of neurocognitive disorder, fracture and mortality were associated with polypharmacy [7–9]. Therefore, the World Health Organization launched the 5-year project 'Medication Without Harm' as part of the Third Global Patient Safety Challenge in 2017 [10].

Cross-country comparison of trends is important to give insight into how to reduce inappropriate polypharmacy as we know that the differences in international polypharmacy trends are related to different strategic initiatives or policies. Indeed, there is substantial variability in the reported prevalence of polypharmacy across countries (e.g. 50% in Ireland and Sweden; <40% in the United States, Australia and New Zealand) [11–17], with a particularly high prevalence observed in the Asian countries (e.g. over 80% in South Korea and Taiwan) [18–20]. However, it is challenging to compare results from published studies because of different study populations, polypharmacy definitions, data sources and medication reimbursement systems [21]. To date, there has been no multinational study using a common study protocol. Thus, we aimed to compare the prevalence and trend of polypharmacy using healthcare data with standardised measurement across five participating sites.

Methods

Study design, data sources and study population

We conducted a multinational, retrospective, time-trend, observational study in the outpatient or community settings of Australia, Hong Kong, Taiwan, South Korea and the United Kingdom using the five databases (Table 1). The study period was between 2013 and 2016, and the study population was patients aged 65 or older not diagnosed with cancer or using medications suggestive of cancer. This approach was adopted to avoid potential overestimation or underestimation of polypharmacy. Each site received ethical approval by the institutional review board (Australia: Monash University Human Research Ethics Committee, 22877; Hong Kong: UW 20-796; South Korea: SKKU 2020-01-007; Taiwan: BER107012; the United Kingdom: 20SRC045). The Australian analysis plan was approved and the manuscript noted by Services Australia.

Polypharmacy definition

We focused on chronic polypharmacy to investigate polypharmacy arising from multimorbidity rather than short-term treatment of acute medical conditions. We defined polypharmacy as the use of ≥5 distinct medications concomitantly for a period of ≥45 days per calendar year, which considered both single prescription- and duration-based definitions simultaneously (Supplementary Figure 1). This definition was selected after reviewing previous literature on polypharmacy definitions applied in research and practice [22, 23].

Statistical analysis

We calculated the annual prevalence of polypharmacy using the number of individuals who experienced polypharmacy at least once as the numerator and the total study population as the denominator, with 95% confidence intervals. We conducted sex- and age-standardisation to address the difference in demographic distribution across study sites using the World Population Prospects 2019 [24]. Changes in trends were evaluated with average annual percentage change (AAPC) using a Poisson regression model, and we conducted sensitivity analyses with different thresholds (≥30 days, ≥60 days) to define polypharmacy. A two-tailed $P < 0.05$ indicates statistical significance, and all analyses

Table 1. Description of database and demographic characteristics in 2016.

	Asia region			Australia	United Kingdom
	Hong Kong	Taiwan	South Korea		
Database	Hospital Authority Data Collaboration Lab	National Health Insurance Database	National Health Insurance Service-National Sample Cohort	Pharmaceutical Benefits Scheme	The IQVIA Medical Research Database
Covered population	0.1 million (1.4%)	2 million (5%)	1 million (2.2%)	2.5 million (10.0%)	18 million (6%)
Healthcare system	Universal	Universal	Universal	Universal	Universal
Enrolled individuals in 2016					
Total (*n*, %)	52,760 (100.0)	253,627 (100.0)	138,838 (100.0)	353,106 (100.0)	819,476 (100.0)
Age group (*n*, %)					
65–69	15,742 (29.8)	89,436 (35.3)	42,868 (32.1)	113,266 (32.1)	214,284 (26.1)
70–74	10,103 (19.1)	52,860 (20.8)	34,178 (24.7)	87,163 (24.7)	183,187 (22.4)
75–79	9,094 (17.2)	46,646 (18.4)	28,702 (17.9)	63,083 (17.9)	138,723 (16.9)
80–84	8,388 (15.9)	31,913 (12.6)	18,684 (12.6)	44,568 (12.6)	110,948 (13.5)
85+	9,433 (17.9)	32,772 (12.9)	14,406 (12.8)	45,026 (12.8)	172,334 (21.0)
Sex (*n*, %)					
Female	28,975 (54.9)	137,344 (54.2)	81,326 (58.6)	187,349 (53.1)	461,261 (56.3)
Male	23,785 (45.1)	116,283 (45.8)	57,512 (41.4)	165,757 (46.9)	358,215 (43.7)

As our databases were collected under the universal healthcare coverage, our results are representative of the entire population in each region or country.

were performed using SAS version 9.4 (SAS Institute Inc, Cary, NC, USA).

Results

Our study cohort included 1.62 million individuals aged ≥ 65 years with a higher proportion of females (Table 1). We observed a difference in the age distribution across the study sites, and more than 30% of the study population was aged ≥ 80 years in Hong Kong and the United Kingdom. In 2016, after the age- and sex-standardisation, the highest overall polypharmacy prevalence was observed in Hong Kong (46.4%), followed by Taiwan (38.8%), South Korea (32.0%), the United Kingdom (23.5%) and Australia (20.1%) (Figure 1). Moreover, we observed a different change in polypharmacy trends across the study sites. There was a steady increase in polypharmacy prevalence in the Asian region, particularly in Hong Kong and South Korea (AAPC: Hong Kong, 2.7%; South Korea, 1.8%; Taiwan, 1.0%). In Australia and the United Kingdom, the trend decreased continuously (AAPC: Australia, −4.9%; the United Kingdom, −1.1%).

Discussion

We found that polypharmacy prevalence was higher and increasing over time in Hong Kong, South Korea and Taiwan. Conversely, polypharmacy prevalence decreased in Australia and the United Kingdom. We found that polypharmacy prevalence was lower than in several previous studies [11, 12, 18–20]. Our findings may be affected by our instrumental definition of polypharmacy. While other studies focused on the number of medications use

only, we additionally considered the continuing duration of multiple drug use to emphasise the burden of medication. Thus, our results should be interpreted in the context of chronic polypharmacy. Consistent with the previous findings [20, 25, 26], our study reaffirms the increasing trends in polypharmacy in Hong Kong, South Korea and Taiwan. Meanwhile, in Australia, a decrease in polypharmacy was reported in 2016 [12], which corresponded with our findings. For the United Kingdom, an increasing trend of polypharmacy was reported from a survey study between 1991 and 2011 [11] and our study found a slightly decreasing trend during the study period. This finding suggests that chronic polypharmacy in older people might have been sustained over the recent years, although there are some differences in the study setting (e.g. study period [1991–2011 versus 2013–16], database [interview versus claims data based] and study region [three regions in England versus all regions in the United Kingdom]).

Polypharmacy should be evaluated in view of its appropriateness within the clinical context of which the medications were prescribed [27]. Australia and the United Kingdom have implemented policy initiatives that may have contributed to decreasing polypharmacy prevalence. Australia now has a National Strategic Action Plan to Reduce Inappropriate Polypharmacy that has been endorsed by bodies including NPS MedicineWise and the Australian Deprescribing Network [28]. Moreover, the Australian Government has funded general practitioners and pharmacists to conduct clinical medication reviews since 2001, with reviews targeted to high-risk patients including those who use five or more medications [29]. Indeed, a substantial decrease in the prevalence of polypharmacy in Australia was observed in 2016, and the previous study suggested that this decrease
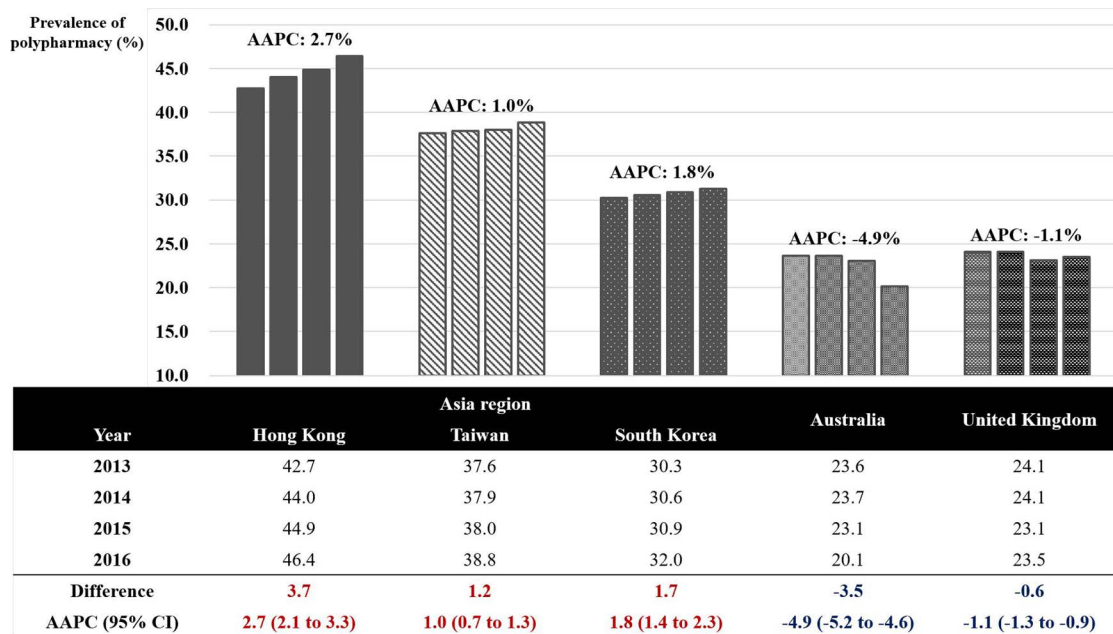
			Asia region		Australia	United Kingdom
Year	Hong Kong	Taiwan	South Korea			
2013	42.7	37.6	30.3		23.6	24.1
2014	44.0	37.9	30.6		23.7	24.1
2015	44.9	38.0	30.9		23.1	23.1
2016	46.4	38.8	32.0		20.1	23.5
Difference	3.7	1.2	1.7		-3.5	-0.6
AAPC (95% CI)	2.7 (2.1 to 3.3)	1.0 (0.7 to 1.3)	1.8 (1.4 to 2.3)		-4.9 (-5.2 to -4.6)	-1.1 (-1.3 to -0.9)

Figure 1. Trend in the age- and sex-standardised prevalence of polypharmacy in participating sites from 2013 to 2016. *Difference was calculated by subtracting the prevalence of the first year from that of the last year. †The change in trend was evaluated by AAPC with a generalised linear model.

was induced by PBS policies influencing a pattern not to prescribe widely used low-cost medications [12]. However, a further study should be conducted on whether this impact was temporary or not. In the United Kingdom, a nationwide consultation service provided by community pharmacists was introduced in 2011 for patients starting a new medicine for chronic disease to prevent inappropriate medication use and enhance adherence [30]. However, our findings cannot be simply interpreted by the aforementioned policy initiatives as other factors (e.g. healthcare accessibility, social inequality) also could influence independently or interactively. In 2017, the United Kingdom organised the National Health Service Clinical Commissioners to provide the safest and most effective treatment to patients by establishing the evidence on the clinical- and cost-effectiveness of medications [31]. In addition, the United Kingdom started the Discharge Medicine Service initiative in 2021 to prevent avoidable harm induced by medication and to provide guidance/materials to support pharmacy contractors [32], showing a continuing and practical effort at the governmental level.

Despite the awareness and efforts to reduce inappropriate polypharmacy, overall increasing trends were observed over a 10-year study period in Hong Kong, Taiwan and South Korea. Of note, Hong Kong had the highest prevalence of chronic polypharmacy (46.4% in 2016) amongst the five study sites with 2.7% annual percentage increase over the study period. Hong Kong has a very well-developed publicly-funded secondary care healthcare system but a relatively poor-developed publicly-funded primary care system. High polypharmacy in Hong Kong may be partially attributable

to patients consulting with multiple specialist doctors in secondary care without a key primary care doctor as a major care provider to coordinate care and prescribing [33, 34]. Furthermore, there is a lack of collaborative models for a medication review.

South Korea, Hong Kong and Taiwan have developed lists of potentially inappropriate medications (PIMs) for older people since early 2010 [35–37]. Taiwan and Hong Kong developed country-specific PIM lists to address the differences in their approved medications, clinical practice and medication accessibility under each healthcare system in 2018 and 2019, respectively [35, 37]. Moreover, South Korea has implemented a pilot project to provide a medication consultation service for patients with multimorbidity, receiving five or more medications based on a collaborative model among physicians, pharmacists and nurses from 2019 [38]. Thus, further studies evaluating the comprehensive impact of these ongoing policy initiatives are warranted.

This study has several limitations. First, we did not consider other important factors, such as education level or socio-economic characteristics, indicating that further trials are needed to address these factors by stratification or standardisation. Second, our findings may have been influenced by the definition of polypharmacy used in our study. However, we observed similar trends in several sensitivity analyses with different thresholds in terms of duration (Supplementary Figures 2 and 3). Third, we measured polypharmacy using dichotomous cut-offs in our study, indicating that quantitative comparison of the number of medications is inappropriate across participating sites. Fourth, the prevalence of polypharmacy could be influenced

by the number of medications included in each participating sites. However, all participating sites have adopted the positive list system based on an economic evaluation with risks and benefits when selecting reimbursed medications. Therefore, we believe that there is no substantial difference in the types of therapeutic areas or individual ingredients across our study sites. Lastly, we did not consider the appropriateness of polypharmacy and a high prevalence of polypharmacy does not necessarily indicate poor practice.

In conclusion, polypharmacy prevalence among older people was higher and increasing over time in Hong Kong, South Korea and Taiwan, compared with Australia and the United Kingdom. Our findings underline the necessity to monitor polypharmacy among older people in Asia by conducting government-level interventions and introducing medicine-optimisation strategies.

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