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Polypharmacy Rates among Patients over 45 years

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Abstract
Polypharmacy, defined as receipt of ≥5 medications in any one month, is often associated with potentially inappropriate prescribing and adverse drug interactions. High levels of polypharmacy have been observed internationally and in Ireland. The Health Service Executive Primary Care Reimbursement Services (HSE-PCRS) pharmacy claims database for the GMS eligible population was used. We conducted Chi-square tests to determine the statistical significance of perceived differences in medication use among patients aged ≥45 years. Our results establish a national benchmark for polypharmacy in gender and various age categories in the HSE-PCRS. Of the 794,628 individuals aged ≥45 years with at least one claim in 2013, 64.3% (510,946) had polypharmacy, with higher rates among women (67.0% - 293,886 - compared to 60.8% of men - 216,444). Patients aged 45-54 years were less likely to have polypharmacy (38.6% - 69,934) compared to those aged 75 years old (82.6% - 197,565). The high levels of polypharmacy are of interest, and suggest that monitoring and evaluation of patients’ medication regimes may be required to ensure appropriateness.

Introduction
The term polypharmacy commonly refers to the concurrent use of five or more medications. Rates of polypharmacy have risen steadily over the last few years¹². The availability of newer treatments and lower thresholds at which certain conditions are now treated has contributed to the increase³, as have health system factors, such as mainly free access to medications, patients’ expectations of their GP and consultations with several doctors⁴. Polypharmacy increases the risks of developing adverse drug reactions, drug-drug interactions, hospitalization, poor quality of life, poor medication adherence and, in some cases, death⁵,⁶. The number of medications is associated with potentially inappropriate prescribing (PIP) and is associated with functional impairment and falls and fractures⁷,⁸.

Higher rates of polypharmacy are found in women and those with lower levels of education²⁴. Advancing age is the greatest predictor of polypharmacy; this is of concern as the elderly are particularly vulnerable to adverse effects due to reduced metabolic and renal functions⁹. Although certain costs may be avoided by increased medication expenditures, polypharmacy continues to present a substantial financial burden to both individuals and the economy at large⁵,¹⁰. The development of policies is required which help ensure multiple medicines are prescribed only to those who actually need them¹¹.
Similar to international rates, the nationally representative (for those over 50) Irish Longitudinal Study on Aging study (TILDA) identified a five percent increase (21.0% to 26.0%) in polypharmacy from wave one to wave two, as well as a steep age gradient (12.0% of those from age 50-64 and 41.0% in those 75)\textsuperscript{12}. Polypharmacy was twice as likely in the lowest wealth quartile compared to the highest and in those with primary or no education compared to those with third level education. Surprisingly, there was no statistical difference by sex. Healthcare utilisation was highest among those who reported polypharmacy; those over 50 years of age constituted 41% of the population, yet were responsible for 79% of inpatient hospital visits, 85% of outpatient hospital visits, and 66% of GP visits\textsuperscript{13}. Older medical card holders were more than three times as likely to report polypharmacy compared to those with no medical coverage or medical insurance; the association remained after controlling for age and number of chronic illnesses\textsuperscript{12}.

Rising rates of polypharmacy in Ireland have been documented\textsuperscript{2} using data from the HSE Primary Care Reimbursement Services (PCRS) pharmacy claims database, Ireland’s national prescription claims database which includes individuals who received reduced prescription medicine under the General Medical Services scheme. Rates of polypharmacy increased dramatically in all age groups from 1997 to 2012, especially older patients (from 17.8% to 60.4% in those aged 65 years). However, this study only included patients from the former Eastern Health Board region in Ireland (which represented only 29.1% of the national population in 2012). The latest year included in their study was 2012. The current study examines the national rate of polypharmacy in 2013, by age and gender; in this way we establish a national benchmark for polypharmacy in the HSE-PCRS and compare our results with those of previous studies in Ireland.

Methods
As eligibility for the HSE-PCRS is based on means and age categories, there is an over-representation of the elderly and children, women, and those from lower socioeconomic groups\textsuperscript{3}. Age and sex profiles as well as detailed information of dispensed prescriptions are available in the database. As all data were anonymised, specific ethical approval for this study was not required. Patients received at least one dispensing of a medicine in 2013 to be included and were aged 45 years old. We categorised patients in the following age groups: 45-54, 55-64, 65-69, 70-74, and 75 years of age. Polypharmacy is defined as the receipt of five or more medications concurrently in any month during 2013. We compare the rates of polypharmacy between age groups and gender using chi-square tests, and significance is assumed at p<0.05. SAS (v9.2) and SPSS (v21.0) were used for statistical analysis.

Results
There were high rates of polypharmacy across all age and gender groups in our analysis (see Table 1). Of the 794,628 patients aged 45 and older receiving at least one medicine in 2013 (17.3% of the Republic of Ireland’s total population), 64.3% had polypharmacy in at least one month. Polypharmacy was more common in women compared to men (67.0% compared to 60.8%); this difference was statistically significant (χ2 (1) =3283.7, p<0.001). Polypharmacy was also significantly associated with increasing age (Table 1); patients aged 45-54 years were less likely to have polypharmacy (38.6%). This proportion
rose steadily through subsequent categories up until the oldest age group (75 years) with 82.6% having polypharmacy ($\chi^2 (4) =93496.0, p<0.001$).

Table 1: Polypharmacy in 2013 by age and sex

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Male</th>
<th>Female</th>
<th>45-54</th>
<th>55-64</th>
<th>65-69</th>
<th>70-74</th>
<th>75</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population (N)</td>
<td>355,992</td>
<td>438,635</td>
<td>181,175</td>
<td>161,310</td>
<td>95,355</td>
<td>166,810</td>
<td>239,183</td>
<td>794,028</td>
</tr>
<tr>
<td>% of study population</td>
<td>44.8</td>
<td>55.2</td>
<td>22.8</td>
<td>20.3</td>
<td>12.0</td>
<td>14.7</td>
<td>30.1</td>
<td>100</td>
</tr>
<tr>
<td>% with polypharmacy</td>
<td>60.8</td>
<td>67.0</td>
<td>38.6</td>
<td>58.1</td>
<td>88.2</td>
<td>71.8</td>
<td>82.6</td>
<td>64.3</td>
</tr>
</tbody>
</table>

Discussion
As no previous studies have looked at polypharmacy rates at the national level in the HSE-PCRS, our results establish a benchmark in this regard. Overall, polypharmacy rates among the GMS eligible population aged 45 years and over in receipt of any medication in 2013 was high (64.3%), almost three times that observed in wave one of TILDA and more than twice as high as that in wave two\textsuperscript{14} (although our results are higher in part due to our comprehensive claims list compared to TILDA’s snapshot of individual medication use). Similar to previous research\textsuperscript{2}, we found that women were more likely to have polypharmacy than men. This was also consistent with international trends. In the TILDA wave one cohort no statistical difference between women and men was found, but this was likely due, in part, to its relatively small sample size compared to the PCRS\textsuperscript{12}. Also, the overrepresentation of women and those from lower socioeconomic groups in the GMS eligible population likely contributes to the discrepancy in statistically significant differences. Women and those from lower socioeconomic status (SES) are known to receive more medicines than men and more affluent individuals\textsuperscript{15}. The SES status of the GMS eligible population is lower than the those in the TILDA cohort, and thus, will have contributed to the higher level of polypharmacy observed for women and men.

The clear age gradient observed in this study, with the lowest level of polypharmacy in the youngest age group and increasing rates with age, is similar to the findings in both international and Irish literature\textsuperscript{2,3,13}. In the first wave of TILDA, polypharmacy increased with age; from 12.0% of adults aged 50-64 years to 41.0% in adults aged 75 years and older. This study found a similar rise, from 38.6% of patients aged 45-54 years to 82.6% of those 75 years of age. It is well established that increasing age is associated with poor health, decreased functional ability and increased demands on the health care system\textsuperscript{16}. Increasing age is associated with an increase in conditions requiring medicines\textsuperscript{3}. Inappropriate prescribing, however, is also more prevalent among those with polypharmacy\textsuperscript{17}. Individuals with polypharmacy and PIP were found to be at risk of developing adverse drug reactions and drug-drug interactions\textsuperscript{6}. Therefore, as polypharmacy rates increase, so does the likelihood of inappropriate prescribing and the associated negative health consequences. As the literature suggests, some of the polypharmacy observed in our study is likely inappropriate\textsuperscript{17,2}, and research has and is
being conducted to investigate the prevalence and consequences of inappropriate prescribing.

Although medication can lessen the burden in the utilization of healthcare by preventing costly hospitalisations and other expensive medical procedures, polypharmacy also contributes to a considerable economic healthcare burden. Eligible GMS patients included in the HSE-PCRS receive prescriptions at only a small co-payment (€2.50 per item). High medication use among these patients contributes to substantial government spending, especially for the oldest age groups. Our results should be considered in light of the fact that a high proportion of medication costs in older adults in Ireland in 2010 (54.5%) were from only 19% of the population. It is likely that some of the polypharmacy observed may result in PIP, and, therefore, there may be room for improvement in the quality of prescribing leading to cost-savings. Interventions which improve the quality of prescribing would benefit patients by eliminating unnecessary costs and unwanted side-effects from PIP, which have significant health and economic implications. Implementing interventions in the Irish population (e.g. medication reviews and pharmacist consultations with patients and physicians) could similarly reduce inappropriate prescribing. Yet, those implementing future intervention efforts should take care to use unbiased measurement tools in determining the effectiveness of interventions.

The very large number of patient cases in the PCRS database greatly strengthened the statistical power of our analysis. However, the HSE-PCRS is only a pharmacy claims database, so it was not possible to determine which medications were actually consumed; also, there was no information on the diagnoses or outcomes associated with polypharmacy. Also, the limited number of variables for analysis available in the HSE-PCRS constrained the breadth of our study.

The high level of polypharmacy observed in Ireland may require intervention, especially in light of the known association with PIP and adverse effects. We recommend research into the mechanisms driving observed polypharmacy, as well as what unintended health consequences they may lead to, especially in light of the potential for prescription cascades, where adverse effects of polypharmacy are treated as symptoms. Overall, our results suggest a need for more thorough monitoring and evaluation of individual medication regimes for appropriateness in each case.

Conflicts of Interest Statement
The authors have no conflicts of interest to declare for this study.

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