Research letters


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Potentially inappropriate medication use among older adults in the USA in 2007

SIR—In this ageing century, potentially inappropriate medication (PIM) use in older adults is a significant patient-safety concern. The Beers criteria, Zhan criteria and Screening Tool of Older Persons’ potentially inappropriate Prescriptions (STOPP) have been widely used for evaluation of healthcare quality and medication safety in older population [1–5]. The Zhan criteria classified 33 drugs into three categories: always inappropriate thus to be avoided (category I), rarely appropriate (II) and for some indications only (III) [2] (please see Table 1 and Appendix 1 in the Supplementary data available in Age and Ageing online on the journal website http://ageing.oxfordjournals.org/). The 33 PIMs are still on the 2002 Beers list and independent of diagnoses or conditions [1], implying the persistent inappropriateness of these drugs.

<table>
<thead>
<tr>
<th>PIMs (Zhan criteria)</th>
<th>Any of 33 PIMs</th>
<th>2007 MEPS</th>
<th>19% MEPS [2]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>% of elderly receiving PIMs (95% CI)</td>
<td>% of elderly receiving PIMs (95% CI)</td>
</tr>
<tr>
<td>Any of 33 PIMs</td>
<td>502</td>
<td>13.84 (12.52–15.17)b</td>
<td>21.3 (19.5–23.1)</td>
</tr>
<tr>
<td>I. Always avoided</td>
<td>46</td>
<td>1.51 (1.06–1.96)b</td>
<td>2.6 (2.0–3.2)</td>
</tr>
<tr>
<td>DICLOROMINE</td>
<td>16</td>
<td>0.63 (0.29–0.97)</td>
<td>0.64</td>
</tr>
<tr>
<td>HYOSYAMINE</td>
<td>15</td>
<td>0.51 (0.24–0.79)</td>
<td>0.37</td>
</tr>
<tr>
<td>II. Rarely appropriate</td>
<td>272</td>
<td>7.62 (6.52–8.72)</td>
<td>9.1 (7.9–10.3)</td>
</tr>
<tr>
<td>DIAZEPAM</td>
<td>34</td>
<td>0.94 (0.57–1.30)</td>
<td>1.37</td>
</tr>
<tr>
<td>PROPPOXYPHEN</td>
<td>144</td>
<td>4.26 (3.39–5.14)</td>
<td>6.21</td>
</tr>
<tr>
<td>CYCOLOBENZAPINE</td>
<td>54</td>
<td>1.31 (0.94–1.68)</td>
<td>1.12</td>
</tr>
<tr>
<td>METAXALONE</td>
<td>20</td>
<td>0.66 (0.33–0.98)</td>
<td>[RSE &gt;30%]</td>
</tr>
<tr>
<td>METHOCARBAZOL</td>
<td>21</td>
<td>0.63 (0.33–0.92)</td>
<td>0.44</td>
</tr>
<tr>
<td>III. Some indications</td>
<td>245</td>
<td>6.41 (5.33–7.29)b</td>
<td>13.3 (11.7–14.9)</td>
</tr>
<tr>
<td>AMITRIPTYLINE</td>
<td>71</td>
<td>1.96 (1.43–2.49)</td>
<td>3.36</td>
</tr>
<tr>
<td>INDOMETHACIN</td>
<td>21</td>
<td>0.52 (0.26–0.78)</td>
<td>0.97</td>
</tr>
<tr>
<td>OXYBUTYNINa</td>
<td>24</td>
<td>0.64 (0.28–1.00)</td>
<td>1.34</td>
</tr>
<tr>
<td>CHLORPHENIRAMINE</td>
<td>26</td>
<td>0.75 (0.37–1.13)</td>
<td>0.50</td>
</tr>
<tr>
<td>HYDROXYZINE</td>
<td>35</td>
<td>0.71 (0.44–0.98)</td>
<td>1.29</td>
</tr>
<tr>
<td>PROMETHAZINE</td>
<td>52</td>
<td>1.47 (1.03–1.91)</td>
<td>1.56</td>
</tr>
<tr>
<td>MUSCLE RELAXANTS AND antispasmodicsa</td>
<td>124</td>
<td>3.35 (2.65–4.04)</td>
<td>Not reported (NR)</td>
</tr>
<tr>
<td>ANTIHISTAMINES</td>
<td>120</td>
<td>3.14 (2.50–3.79)</td>
<td>NR</td>
</tr>
<tr>
<td>GASTROINTESTINAL antispasmodicsa</td>
<td>35</td>
<td>1.29 (0.84–1.73)</td>
<td>NR</td>
</tr>
<tr>
<td>LONG-ACTING benzodiazepinesa</td>
<td>43</td>
<td>1.14 (0.71–1.57)</td>
<td>NR</td>
</tr>
</tbody>
</table>

CI, confidence interval; MEPS, Medical Expenditure Panel Survey; RSE, relative standard error.

aFor the complete list, please see Appendix 1 in the Supplementary data available in Age and Ageing online on the journal website http://ageing.oxfordjournals.org/.
bThe differences between 1996 and 2007 are statistically significant because the 95% CIs are not overlapped.
The US National Healthcare Quality and Disparities Reports (NHQR and NHDR, respectively) have adopted the Zhan criteria since 2003 as one of the medication-safety measures in older adults [6]. However, the government reports lack detailed information on specific PIMs. This study was designed to determine the most recent PIM-use prevalence using 2007 Medical Expenditure Panel Survey (MEPS) for each medication and category, to compare the prevalence between 1996 and 2007 and to identify risk factors for the PIM use.

Methods

The detailed information on the MEPS databases and variable constructs can be found in the Appendix 2, Supplementary data available in Age and Ageing online. The study subjects were those community-dwelling adults aged 65 or older (n = 3,570, representing 38.9 million non-institutionalised aged population). Among the independent variables, the number of prescriptions includes all prescribed medications initially purchased or otherwise obtained as well as any refills. The median number of prescriptions for the older patients having at least 1 prescription was 25 (inter-quartile range, 35) in 2007 (n = 3,224), while it was 14 in 1996 [2]. Number of prescriptions is a proxy measure for polypharmacy. This study used publicly available, de-identified data and thus was exempt from the institutional review board review.

Statistical analyses

The prevalence rates of PIM use in 1996 and 2007 were compared using their 95% confidence interval (CI) estimates (Table 1 and Appendix 1 in Supplementary data available in Age and Ageing online). If the CIs were not overlapped, then the rates were statistically significantly different. If the national estimates had relative standard errors (RSEs) greater than 30%, they were considered unreliable [2, 6, 7]. Wald Chi-square ($\chi^2$) tests were used to assess the differences in the use of 33 PIMs by respondents’ characteristics (Supplementary data are available in Age and Ageing online, Appendix 3). Logistic regression was used to examine the contributing factors for the PIM use (Supplementary data are available in Age and Ageing online, Appendix 4). All tests were two-sided, with the predetermined statistical significance at alpha level of 0.05. Statistical analyses were conducted using SAS version 9.1.3 (SAS Institute, Inc., Cary, NC, USA). The survey procedures including SURVEYFREQ and SURVEYLOGISTIC were used to account for the complex sample design of the MEPS.

Results

While the aged population increased from 1996 (32.3 million [2]) to 2007, the number of community-dwelling older adults who received at least 1 of the 33 PIMs decreased from 6.9 million [2] to 5.4 million. Table 1 and Supplementary data available in Age and Ageing online, Appendix 1 present the numbers of the older adults who used the PIMs in 2007 and compare their percentages between 1996 and 2007. The proportions of older adults using the 33 PIMs and categories I and III drugs significantly decreased. The top three most often misused PIMs did not change, which were propoxyphene, amitriptyline and promethazine. The most often misused medications and medication classes in 2007 also included muscle relaxants and antispasmodics, anticholinergics and antihistamines, gastrointestinal antispasmodics, long-acting benzodiazepines and indomethacin.

The maximum number of PIMs received by an individual in 2007 was three (Table 2), less than the number of five in 1987 (only 20 PIMs examined then) [8]. The most common combination was propoxyphene plus amitriptyline. Appendix 3, Supplementary data available in Age and Ageing online, displays the prevalence rates of prescription drug utilisation and PIM use in the older Americans by respondents’ characteristics. Nearly 90% of the elderly had at least one prescription in 2007. After controlling for other factors, the logistic regression model (Supplementary data available in Age and Ageing online, Appendix 4) showed that sex, family income, educational level, census region, number of prescriptions and self-rated health status were significant predictors of the 33 PIMs use. Older women, people taking ≥25 prescriptions, people with middle family income, people living in the South census region, and people who said they were in fair or poor health were more likely to have received an inappropriate medication during the year than older men, people taking <25 prescriptions, and people in other income, region or health status groups. No significant racial or ethnic disparities in the 33 PIMs use were found, while race or ethnicity was significantly associated with the use of the 33 PIMs in 1996 (not significant for the category-I’s 11 PIMs use) [2].

Discussion

The utilisation prevalence of the 33 PIMs on the Zhan list among older Americans decreased significantly between 1996 and 2007. It is a further reduction comparing with
previous findings [2, 6]. Such achievements may result from various interventions such as the dissemination of explicit PIM criteria [1, 2, 9]. However, we should note that more than 10% of the US non-institutionalised older adults still received at least 1 of the 33 PIMs, and the use of some PIMs continued to be problematic.

Propoxyphene was the most commonly misused drug in 2007, whose misuse did not change much over the years [2, 10–13]. Propoxyphene-containing products offer few analgesic advantages over aspirin or acetaminophen, yet it may cause central nervous system toxicity, adverse drug–drug interactions and deaths [1, 13–15]. Following the European Medicines Agency’s phased withdrawal decision in June 2009 [15], the US Food and Drug Administration (FDA) decided to add a black box warning to the drug label. In November 2010, with the new safety-study results confirming the cardiotoxicity, the FDA announced the propoxyphene removal from the US market [16]. Also, attention should be paid to other medications and medication classes, including amitriptyline, muscle relaxants, antihistamines, gastrointestinal antispasmodics, diazepam and indomethacin. Most of the drugs are so outmoded that they would have been retired years ago. The continuing, imperfect use was ‘the triumph of habit over evidence in shaping drug prescribing choices’ [17]. A step forward in reducing or eliminating such medications use in older adults is required.

Comparing with previous reports [2, 8, 12], similar at-risk older subpopulations for PIM use were identified: women, those who rated their health status as fair and poor, people living in the South census region (not a significant factor in 1996-MEPS study [2]), and patients having more prescriptions. Studies have highlighted polypharmacy a significant risk factor for PIM use [2, 8, 9, 18]. Auditing drug regimens and a parsimonious prescribing style might be helpful for reducing polypharmacy and prevalence of PIM use [8, 18]. The strong geographic disparity indicates a wide difference in prescribing patterns across the USA. The fact that risk factors for PIM use did not change may imply that more effective interventions are urgently needed. Such interventions should be firstly focused on the persistently vulnerable subgroups, and further research is necessary to determine the underlying causes of the disparities. With the first baby boomers turning 65 this year, rapid responses are required from the US geriatric medicine community.

Our study has some limitations. First, an important concern is the controversial PIM criteria including the Zhan criteria [1, 2, 18, 19]. For the purpose of prevalence comparison between 1996 and 2007, we did not use the updated Beers or STOPP criteria which include more and newer PIMs. However, because the Zhan criteria are somewhat obsolete, the results should be interpreted with caution. The decline in the 33 PIMs use is not adequate to conclude that the overall PIM use in the USA has improved greatly. In addition, we did not assess drug–disease interactions, drug–drug interactions and other drug use problems such as medication under-use [2, 20]. These limitations may make our estimates unreliable. Second, we cannot identify whether the decline of PIM use in older population is parallel to that in non-elderly population. Physicians could just be retiring the old drugs in both the older and non-elderly populations. Further research may be focused on the possible decline in the utilisation of these drugs among the non-elderly population, and compare it to the study findings in the older population.

Third, under given circumstances, an inappropriate medication might be appropriately prescribed, dispensed and administered [2, 18]. Since medication dose, frequency and duration were not reported in the MEPS, we included all the drugs despite dose, frequency or duration. Thus we may overestimate the PIM use to some extent. Fourth, all the information used in the study is from self-reported surveys. The respondents’ recall bias and social desirability in answering questions, and the survey sampling and data entry/ascertainment problems may affect the data accuracy. Fifth, the estimates for drugs with RSEs greater than 30% were not reliable. However, the goal of monitoring PIM use is to reduce and eliminate it, not to make reliable national estimation.

Key points

- Prevalence of the 33 PIMs use among the older adults in the USA decreased from 1996 to 2007 in terms of the Zhan criteria.
- Propoxyphene, amitriptyline, antihistamines, diazepam, muscle relaxants, gastrointestinal antispasmodics and indomethacin were still prevalent among older adults in the USA in 2007.
- More effective interventions to further improve medication use in older patients, specifically in those priority subpopulations with high-risk factors, are required.

Conflicts of interest

None declared.

Supplementary data

Supplementary data mentioned in the text is available to subscribers in Age and Ageing online.
References


Estimating GFR in the oldest old: does it matter what equation we use?

SIR—In coming decades, the Western world will face an epidemic of ageing. This forthcoming ‘grey epidemic’ will lead to an explosion of chronic diseases like chronic kidney disease (CKD). CKD is an important public health problem for several reasons. First, the prevalence of CKD is high [1], especially among patients aged 70 years and older [2]. Second, knowledge of the actual glomerular filtration rate (GFR) of a patient has important consequences in terms of medication, as the dosages of many drugs should be adapted according to renal function [3]. Finally, the cost and the burden of renal replacement therapy are high.

Measurement of the GFR is the gold standard index of overall kidney function. Several equations derived from endogenous filtration markers were developed to estimate this GFR. However, the most accurate method for estimating GFR, especially in elderly patients, is topic of on-going debate [4]. A recent systematic review [5] showed that the modification of diet in renal disease (MDRD) equation [6] does not differ appreciably from the Cockcroft–Gault equation [7] in terms of the accuracy with which GFR is estimated and that there is limited but promising evidence concerning serum cystatin C level as a biomarker of kidney function in the oldest of the old [8, 9]. In the absence of well-validated equations, a variety of equations are currently used in research as well as in clinical practice to estimate GFR in the elderly.

Therefore, this study was designed to determine differences in GFR estimated according to various equations in elderly patients and to investigate the clinical relevance of these differences at an individual patient level.

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