High Prevalence of Poor Quality Drug Prescribing in Older Individuals: A Nationwide Report From the Italian Medicines Agency (AIFA)

Graziano Onder,1 Stefano Bonassi,2 Angela M. Abbatecola,3 Pietro Folino-Gallo,4 Francesco Lapi,5 Niccolò Marchionni,6 Luca Pani,4 Sergio Pecorelli,4 Daniele Sancarlo,7 Angelo Scuteri,9 Gianluca Trifirò,6 Cristiana Vitale,2 Stefano Maria Zuccaro,10 Roberto Bernabei,1 and Massimo Fini2; on behalf of the Geriatrics Working Group of the Italian Medicines Agency (AIFA)

1Department of Geriatrics, Centro Medicina dell’Invecchiamento, Università Cattolica del Sacro Cuore, Rome, Italy. 2Scientific Direction, IRCCS San Raffaele Pisana, Rome, Italy. 3Scientific Direction, Italian National Research Center on Aging (INRCA), Ancona, Italy. 4Agenzia Italiana del Farmaco (AIFA), Rome, Italy. 5Department of Preclinical and Clinical Pharmacology, University of Florence, Italy. 6Unit of Gerontology and Geriatric Medicine, University of Florence, Italy. 7Department of Medical Sciences, IRCCS Casa Sollievo della Sofferenza, San Giovanni Rotondo, Foggia, Italy. 8UOC Geriatria, Italian National Research Center on Aging (INRCA), Rome, Italy. 9Department of Clinical and Experimental Medicine, University of Messina, Italy. 10UOC Geriatria, Ospedale Israelitico, Rome, Italy.

Address correspondence to Graziano Onder, MD, PhD, Centro Medicina dell’invecchiamento, Dipartimento di Scienze Gerontologiche, Geriatriche e Fisioterapiche, Università Cattolica del Sacro Cuore, Largo F. Vito 1, 00168 Roma, Italy. Email: graziano_onder@rm.unicatt.it

Background. Poor quality of drug prescribing in older persons is often associated with increased drug-related adverse events, hospitalization, and mortality. The present study describes a set of prescribing quality indicators developed by the Geriatrics Working Group of the Italian Medicines Agency (AIFA) and estimates their prevalence in the entire elderly (≥65 years) population in Italy.

Methods. We performed a cross-sectional study using 2011 data from the OsMed (Osservatorio dei Medicinali) database, which comprises all prescribed drugs that are reimbursed by the Italian National Healthcare System. Yearly prevalence of drug prescribing quality indicators in the Italian older population (n = 12,301,537) was determined.

Results. Overall, 13 quality indicators addressing polypharmacy, adherence to treatment of chronic diseases, prescribing cascade, undertreatment, drug–drug interactions, and drugs to be avoided were identified. Polypharmacy was common, with more than 1.3 million individuals taking greater than or equal to 10 drugs (11.3% of the study population). The prevalence of low adherence and undertreatment was also elevated and increased with advancing age, with highest prevalence occurring in individuals aged 85 years and older. Prevalence was less than 3% for quality indicators assessing the prescribing cascade, drug–drug interactions, and drugs to be avoided.

Conclusions. These results confirm the high frequency of suboptimal drug prescribing in older adults, using a database that covers the whole Italian population. In general, this descriptive study may help in prioritizing strategies aimed at improving the quality of prescribing in elderly population.

Key Words: Quality indicators—Prescribing—OsMed.

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Poor quality of prescribing is associated with increased risk of drug-related adverse events in the elderly population, including hospitalization and mortality (1). In the past decades, different sets of indicators have been developed in order to provide a measure of prescribing performance and, hence, to assess the quality of care in older populations and its changes over time (2–7).

It has been widely shown that suboptimal prescribing is very common, with a prevalence ranging from 12% to 40%, due to different settings and sets of indicators used (8–12). In general, these indicators cannot replace clinical judgment, but they represent a valuable tool to rapidly assess and compare the quality of prescribing in different populations and settings over time. Most available prescribing indicators have been developed to identify drugs to be avoided, whereas other important parameters of prescribing quality, including treatment adherence, drug–drug interactions, and prescribing cascade, have been rarely
Literature was searched in the MeSH the panel had a recognized expertise in geriatric medicine, appointed a 12-member panel, named GWG. Members of articles. The quality of drugs prescribing in older adults were revised (quality of indicators and criteria to assess the additional relevant references. Moreover, previously published sets of quality indicators in the elderly population. These indicators are intended to be used as the basis for medication use control programs and to design educational interventions to improve drug prescriptions nationwide. The database of the Medicines Monitoring Center (Osservatorio dei Medicinali, OsMed) (15), which tracks all drugs dispensed and reimbursed by the National Healthcare System (NHS) in Italy (about 1.8 billion in year 2011), provides a unique opportunity to evaluate the actual prevalence of a set of indicators that are deemed to be most critical in assessing the quality of prescriptions in elderly population. This article presents the prevalence of a set of 13 indicators of drug prescribing quality in the Italian elderly population over the year 2011 that have been developed by the GWG experts.

METHODS

Quality Indicators Development

Quality indicators were developed across three steps.

Step 1: Literature search.—Literature was searched in the PubMed database (National Library of Medicine, National Institutes of Health, Bethesda, MD), using the keywords drugs, elderly, quality indicators in the MeSH (Medical Subject Headings). The search was extended through September 2011. Non-English articles and letters to the editor, commentaries, review articles, editorials, and observational studies were included. Articles dealing with prescribing quality indicators or criteria to assess suboptimal prescribing in the elderly population were selected. All retrieved articles were systematically analyzed to identify additional relevant references. Moreover, previously published sets of quality indicators and criteria to assess the quality of drugs prescribing in older adults were revised (2–7). This literature search process was performed by two researchers (G.O. and S.B.) and led to the selection of 275 articles.

Step 2: Quality indicators rating and selection.—AIFA appointed a 12-member panel, named GWG. Members of the panel had a recognized expertise in geriatric medicine, pharmacy practice, research, and quality measures and they represented different settings (long-term care, academic and nonacademic hospitals, primary care). Members of the panel applied a modified Delphi method to the systematic review to reach consensus on prescribing quality indicators. Selected articles were discussed in plenary sessions of the panel, and a preliminary list of 74 quality indicators was identified. The technical possibility of measuring each of them in the OsMed database was then explored. Indicators addressing drug classes not captured by the OsMed database (ie, drugs not reimbursed by the NHS, over the counter drugs, and drugs dispensed in hospital) were excluded. This selection procedure generated a reduced list of 36 quality indicators. Each of these indicators was then examined by panel members, who rated each indicator on a 0–5 scale according to (a) clinical relevance to older patients and (b) availability of evidence showing an association of the quality indicator with hard outcomes in older adults. Ratings were tallied and returned to the panel. Two 1-day meetings allowed for review of survey ratings, discussion, and consensus building. A total of 13 indicators were finally selected.

Step 3: Development of quality indicators templates.—Each quality indicator was included in a specific form and characterized through the following items: (a) aim, (b) rationale, (c) clinical relevance, (d) definition (including the coding algorithm), (e) limitations, and (f) references (see Supplementary Appendix 1).

OsMed Database

The prevalence of the 13 quality indicators in the Italian population aged 65 or older was measured in the OsMed database (15). The Italian NHS provides all residents with economic coverage of drugs with documented clinical efficacy used for treating serious and chronic diseases (16). OsMed includes the data for all drug prescriptions reimbursed by the NHS that are dispensed by approximately 18,000 pharmacies across Italy (15). In OsMed database, information on each drug package, identified via Anatomical Therapeutic Chemical classification and ID package unique identifier codes, is tracked at individual level but are concealed to guarantee patient privacy. Using the OsMed database, a report on drug use in Italy is published yearly by AIFA (15) with the following objectives: (a) to describe drug consumption at national level, (b) to examine changes in drug use over time, and (c) to benchmark drugs consumption across different Italian regions.

Italian Pharmaceutical Reimbursement System

The Italian pharmaceutical reimbursement system covers all relevant diseases and the whole country providing universal pharmaceutical coverage to the whole population.
The general conditions of the reimbursement system are established on a national level. Reimbursed drugs (known as Class A) include essential drugs and drugs for serious, acute, and chronic diseases (ie, antihypertensive drugs, antibiotics, hypoglycemic agents, antibiotics, antidepressants, antiaggregants, anticoagulants, anti-Parkinson drugs, etc.). Nonreimbursed drugs (known as Class C) include drugs for disease of slight importance and for minor ailments, drugs whose use is discouraged and drug not requiring a medical prescription (ie, benzodiazepines, antispasmodics, topical treatments, etc.).

Data Analysis

Analysis was limited to drugs dispensed in year 2011. The prevalence of quality indicators was calculated by dividing the number of patients with at least one treatment episode that met the criteria described in the quality indicator, by the overall number of Italian older individuals reported by the National Institute of Statistics in January 2011 (n = 12,301,537) (17).

The description, definition, and clinical relevance of the 13 quality indicators developed by the GWG are presented in Table 1.

Polypharmacy (Indicator 1) was defined as a two-level indicator: dispensing of 5–9 or greater than or equal to 10 different drugs (Anatomical Therapeutic Chemical—fifth level) within the same quarter of year 2011. The number of medicines dispensed in each quarter was calculated, and the highest number of drugs dispensed in a single quarter was used to define polypharmacy over the 1-year period.

Four indicators were designed to evaluate adherence to most common chronic treatments, that is, antihypertensive, hypoglycemic, antiosteoporotic, and antidepressant drugs (Indicators 2–5). To calculate adherence, older adults who were newly prescribed with one of the drugs in the classes of interest between July 1 and December 31, 2010, were identified, and the date of first drug dispensing was defined as the index date. Patients were considered as newly treated if they had no dispensing of any drug of the same class over the 6 months before the index date. Adherence was estimated by calculating the proportion of days covered by drugs dispensed during a period of 182 or 365 days, respectively, for antidepressants or for all other drug classes. The number of days covered by each dispensing was calculated by dividing the total amount of active drug in each dispense (quantity of active principle in the specific package multiplied by the number of dispensed packages) by the recommended defined daily dose. In accordance with previously adopted thresholds, low adherence was defined as proportion of days covered less than 40% (18,19).

Prescribing cascade refers to the process whereby the side effect of drugs is misdiagnosed as symptoms of another problem resulting in further prescriptions. The concomitant dispensing of antipsychotic and anti-Parkinson drugs within one or more quarters of 2011 was used as an indicator of prescribing cascade (Indicator 6). This was done because parkinsonism is a possible side effect of antipsychotics and, conversely, the use of anti-Parkinson agents may trigger behavioral disorders (20–22). Therefore, the concomitant prescription of antipsychotic and anti-Parkinson agents may represent an example of a prescribing cascade, independently of the drug having been prescribed first.

Undertreatment (Indicator 7) was assessed as the proportion of patients who were not prescribed statins among those considered as diabetics because they had been using two or more hypoglycemic drugs in 2011. The concomitant prescription of drugs increasing the risk of bleeding, nephrotoxicity and/or hyperkalemia, or QT prolongation within one or more quarters of 2011, was taken into account for assessing potential drug–drug interactions (Indicators 8–10). For QT prolonging drugs, only those with a risk of Torsades de Pointes (substantial evidence supports the conclusion that these drugs prolong the QT interval and have a risk of Torsades de Pointes when used as directed in labeling), as reported in Arizona Cert list (23), were taken into account.

Use of drugs to be avoided was explored over one or more quarters (Indicators 11–12), or over the whole year 2011 (Indicator 13). Indicator 11, represented by use of antihypertensive drugs with unfavorable risk–benefit profile, was measured as the proportion of patients with (a) any dispensing of either short-acting calcium antagonists or (b) dispensing of doxazosin or clonidine or methylidopa not in combination with other antihypertensive agents. Indicator 12 assessed the use of high dosage of digoxin (defined as a daily dose > 0.125 mg). Indicator 13 evaluated the proportion of patients with at least one dispensing of chlorpropamide or glibenclamide at any time. The list of Anatomical Therapeutic Chemical codes used to identify drugs included in quality indicators is available in Supplementary Appendix 1.

Results

During year 2011, the OsMed database collected data on drugs dispensed to 11,593,989 individuals aged 65 years or older, representing 94.2% of the Italian residents of this age group, as reported by the Italian National Institute of Statistics (n = 12,301,537). Of the total older population included in the OsMed database, 5,726,208 individuals were 65–74 years, 4,286,993 were 75–84 years, and 1,580,788 were 85 years or more of age, representing, respectively, the 93.0%, 95.8%, and 94.5% of the Italian population in the same age groups.

Table 2 shows the prevalence of quality indicators in the study population. Polypharmacy was common, with more than 1.3 million individuals (11.3%) receiving a simultaneous prescription of greater than or equal to 10 drugs. In particular, the group aged 75–84 years was exposed to the
Table 1. Description, Definition, and Relevance of Quality Indicators

<table>
<thead>
<tr>
<th>Description</th>
<th>Definition</th>
<th>Clinical Relevance in Older Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polypharmacy</td>
<td>Concomitant dispensing of: a. 5–9 drugs b. ≥10 drugs</td>
<td>Presence of multiple chronic conditions requires long-term treatment with complex drug regimens</td>
</tr>
<tr>
<td>Treatment adherence</td>
<td>&lt;40% of days covered by dispensed antidepressant drugs over a 6-mo period</td>
<td>High prevalence of these diseases among older adults Factors limiting adherence (sensory deficits, cognitive and functional deficits, depression, polypharmacy) are common in older adults</td>
</tr>
<tr>
<td>2. Low adherence to antihypertensive drugs</td>
<td>&lt;40% of days covered by dispensed antihypertensive drugs over 1-y period</td>
<td>Low adherence reduces substantially the effectiveness of drug treatment</td>
</tr>
<tr>
<td>3. Low adherence to hypoglycemic drugs</td>
<td>&lt;40% of days covered by dispensed hypoglycemic drugs over 1-y period</td>
<td>Low adherence reduces substantially the effectiveness of drug treatment</td>
</tr>
<tr>
<td>4. Low adherence to antosteoporotic drugs</td>
<td>&lt;40% of days covered by dispensed antosteoporotic drugs over 1-y period</td>
<td>Low adherence reduces substantially the effectiveness of drug treatment</td>
</tr>
<tr>
<td>Prescribing cascade</td>
<td>Concomitant dispensing of antidepressant and antipsychotic drugs</td>
<td>Approximately 25% of all cases of parkinsonism in the elderly population are caused by drugs In case of antipsychotic-induced parkinsonism, treatment with antipsychotic should be modified (if not possible to withdraw it) instead of adding an anti-Parkinson drug Anti-Parkinson agents can cause behavioral disorders</td>
</tr>
<tr>
<td>Undertreatment</td>
<td>Lack of dispensing of statins in older adults on hypoglycemic drugs</td>
<td>High prevalence of diabetes among older adults Statins are recommended in diabetic patients for cardiovascular prevention</td>
</tr>
<tr>
<td>Drug–drug interaction</td>
<td>Concomitant dispensing of warfarin in combination with either traditional NSAIDs/COX-2 inhibitors or low dosage aspirin/another antiplatelet drugs</td>
<td>Older adults are at increased risk of bleeding (especially, at gastrointestinal level) Synergistic effect of concomitant use of drugs with high bleeding risk is potentially detrimental</td>
</tr>
<tr>
<td>8. Concomitant use of drugs increasing the risk of bleeding</td>
<td>Concomitant dispensing of ACE inhibitors/ARB and aldosterone antagonists and traditional NSAIDs/COX-2 inhibitors</td>
<td>Older persons are particularly susceptible to the drug-related nephrotoxicity due to physiological renal function impairment with advancing age</td>
</tr>
<tr>
<td>9. Concomitant use of drugs increasing the risk of renal failure and/or hyperkalemia</td>
<td>Concomitant dispensing of ≥2 drugs that may induce Torsades de Pointes</td>
<td>Advanced age is associated with factors that may prolong QT interval such as heart disease and hypokalemia QT prolongation may evolve to Torsades de Pointes and fatal ventricular fibrillation</td>
</tr>
<tr>
<td>10. Concomitant use of ≥2 QT prolonging drugs</td>
<td>Dispensing of either doxazosin, clonidine, or methyldopa as monotherapy or any dispensing of short-acting calcium antagonists</td>
<td>High prevalence of hypertension among older adults These drugs are considered second choice due to their side effects and limited efficacy in preventing/treating target organ damage</td>
</tr>
<tr>
<td>Drugs to be avoided</td>
<td>Dispensing of digoxin &gt; 0.125 mg/d</td>
<td>High dose of digoxin associated with potentially detrimental reduced renal clearance, electrolyte alterations, and reduced lean body mass. Higher the dosage of digoxin, higher its potential for pharmacological interaction Digoxin has a very narrow therapeutic index</td>
</tr>
<tr>
<td>11. Use of antihypertensive drugs with unfavorable risk–benefit profile</td>
<td>High prevalence of hypoglycemia</td>
<td>Reduced renal clearance increases risk of hypoglycemia when using drugs with long half-lives and renal excretion</td>
</tr>
<tr>
<td>12. Use of high dosage of digoxin</td>
<td>Dispensing of chlorpropamide or glibenclamide</td>
<td>High prevalence of hypoglycemia These drugs are considered second choice due to their side effects and limited efficacy in preventing/treating target organ damage</td>
</tr>
<tr>
<td>Notes: ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blockers; COX-2 inhibitors = cyclooxygenase-2 inhibitors; NSAIDs = nonsteroidal anti-inflammatory drugs.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quality Indicator</td>
<td>All Age Groups (≥65 y), n = 12,301,537 (%)</td>
<td>65–74 y, n = 6,154,421 (%)</td>
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<tr>
<td>----------------------------------------------------------------------------------</td>
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<tr>
<td>1. Polypharmacy</td>
<td></td>
<td></td>
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<tr>
<td>5–9 drugs</td>
<td>6,024,383 (49.0)</td>
<td>2,681,639 (43.6)</td>
</tr>
<tr>
<td>≥10 drugs</td>
<td>1,389,591 (11.3)</td>
<td>529,506 (8.6)</td>
</tr>
<tr>
<td>2. Low adherence to antidepressant drug treatment*</td>
<td>201,290 (63.9)</td>
<td>83,110 (62.6)</td>
</tr>
<tr>
<td>3. Low adherence to antihypertensive drug treatment*</td>
<td>179,975 (46.4)</td>
<td>84,983 (43.2)</td>
</tr>
<tr>
<td>4. Low adherence to hypoglycemic drug treatment*</td>
<td>92,017 (63.0)</td>
<td>44,227 (63.0)</td>
</tr>
<tr>
<td>5. Low adherence to antosteoporotic drug treatment*</td>
<td>56,621 (52.4)</td>
<td>24,424 (48.7)</td>
</tr>
<tr>
<td>6. Use of anti-Parkinson and antipsychotic drugs</td>
<td>25,949 (0.2)</td>
<td>10,200 (0.2)</td>
</tr>
<tr>
<td>7. Underutilization of statins in diabetic patients (as % of the whole elderly population)</td>
<td>918,662 (7.5)</td>
<td>418,257 (6.8)</td>
</tr>
<tr>
<td>As % of the elderly population on hypoglycemic drugs</td>
<td>53.4</td>
<td>48.3</td>
</tr>
<tr>
<td>8. Concomitant use of drugs increasing the risk of bleeding</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Warfarin + traditional NSAIDs/COX-2 inhibitors</td>
<td>178,458 (1.5)</td>
<td>64,939 (1.1)</td>
</tr>
<tr>
<td>Warfarin + aspirin/antiplatelets</td>
<td>100,236 (0.8)</td>
<td>38,953 (0.6)</td>
</tr>
<tr>
<td>Warfarin + NSAIDs/COX-2 inhibitors + aspirin/antiplatelets</td>
<td>22,174 (0.2)</td>
<td>8,574 (0.1)</td>
</tr>
<tr>
<td>9. Concomitant use of drugs increasing the risk of renal failure and/or hyperkalemia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(ACE inhibitors/ARB + aldosterone antagonists + NSAIDs/COX-2 inhibitors)</td>
<td>85,412 (0.7)</td>
<td>28,860 (0.5)</td>
</tr>
<tr>
<td>10. Concomitant use of ≥2 QT prolonging drugs‡</td>
<td>36,359 (0.3)</td>
<td>13,580 (0.2)</td>
</tr>
<tr>
<td>11. Use of antihypertensive drugs with unfavorable risk–benefit profile (doxazosin, clonidine, or methylkopa as monotherapy or any use of short-acting calcium antagonists; as % of the whole elderly population)</td>
<td>196,690 (1.6)</td>
<td>88,069 (1.4)</td>
</tr>
<tr>
<td>As % of the elderly population on antihypertensive drugs‡</td>
<td>2.5</td>
<td>2.3</td>
</tr>
<tr>
<td>12. Use of high dosage of digoxin (&gt;0.125 mg/d)</td>
<td>47,314 (0.4)</td>
<td>16,323 (0.3)</td>
</tr>
<tr>
<td>13. Use of oral hypoglycemic agents associated with high risk of hypoglycemia</td>
<td>87,755 (0.7)</td>
<td>35,786 (0.6)</td>
</tr>
<tr>
<td>(chlorpropamide or glibenclamide; as % of the whole elderly population)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>As % of the elderly population on hypoglycemic drugs†</td>
<td>5.1</td>
<td>4.1</td>
</tr>
</tbody>
</table>

Notes: ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blockers; COX-2 inhibitors = cyclooxygenase-2 inhibitors; NSAIDs = nonsteroidal anti-inflammatory drugs.

*Prevalence has been calculated for newly treated participants only (Indicator 2: n = 315,015; Indicator 3: n = 388,079; Indicator 4: n = 146,094; Indicator 5: n = 108,037). Low adherence is defined as proportion of days covered < 40%.

†n = 1,721,767.

‡List of drugs that are well known to carry a risk of Torsades de Pointes, as reported in Arizona Cert list (available at [http://www.azcert.org/medical-pros/drug-lists/drug-lists.cfm](http://www.azcert.org/medical-pros/drug-lists/drug-lists.cfm), accessed January 2012).

§n = 7,999,099.
highest pharmacological burden, with 55.0% and 14.1% of individuals receiving 5–9 drugs and greater than or equal to 10 drugs, respectively. Low adherence to chronic treatments with antidepressants, antihypertensives, hypoglycemic, or antosteoporotic agents was also frequent and increased with advancing age, with highest prevalence (from 56.1% to 70.1%) in individuals aged 85 or more. Undertreatment with statins was observed in 53.4% of diabetic individuals (more than 70% in the group aged 85 years or more), occurring in more than 900,000 older adults. Prescribing cascade, potential drug–drug interactions, and drugs to be avoided all had a prevalence less than 3% but, in absolute terms, they accounted for 22,000–196,000 individuals. The prevalence of use of antihypertensive drugs with unfavorable risk–benefit profile, including doxazosin, clonidine, or methyldopa as monotherapy or any use of short-acting calcium antagonists (Indicator 11), was 1.6% in the population as a whole, but increased to 2.5% when analysis was restricted to individuals on antihypertensive drugs. Similarly, the prevalence of use of oral hypoglycemic agents associated with high risk of hypoglycemia, including chlorpropamide and glibenclamide (Indicator 13), was only 0.7%, but increased to 5.1% when only individuals on hypoglycemic drugs were taken into account.

**Discussion**

In this study, we aimed to analyze, using an original set of indicators, a database of more than 1 billion drugs dispensed in year 2011. We specifically evaluated the quality of drug prescribing to the older (65+ years of age) Italian population. Although these newly designed indicators do not cover the broader range of suboptimal drug prescribing, they represent a useful tool to better assess and monitor nationwide the quality of drug use in the older population. The information provided by these indicators allows the identification of critical issues concerning drug prescribing in older adults. Because quality indicators were applied to the OsMed national database, which tracks virtually all the dispensed drugs that are covered by the NHS in Italy, they provide a representative picture of pharmacological treatment in the whole Italian older population. Indeed, this approach allowed for a quantitative assessment of the quality of drug prescribing and is expected to provide a description more accurate than estimates and projections based on population samples.

Findings of the present study may be a basis for future studies aimed at implementing health policies and educational efforts to improve prescription patterns worldwide. Highly prevalent quality indicators, including polypharmacy and poor adherence, might be addressed by particular interventions, for example, by providing prescribing guidance and tools to support the delivery of effective medication reviews with rationalization of prescribing needs and effective communication of outcomes to patients and all prescribers involved in providing care. These interventions will be developed in the context of the Action Group A1 of the European Innovation Partnership on Active and Healthy Ageing supported by the European Commission, which is focused on activities and pilot initiatives, joint efforts and synergies across European countries, to increment active life expectancy and reduce disability through the improvement of prescribing quality and adherence to drug treatment (24).

The set of indicators proposed by the AIFA GWG were developed to provide an explicit and meaningful measure of the quality of prescribing in a real-world perspective. In particular, the set assessed six domains (polypharmacy, adherence, prescribing cascade, undertreatment, potential drug–drug interaction, drugs to be avoided), identifying the occurrence of erroneous or risky prescriptions and suboptimal prescribing (1). Polypharmacy resulted to be extremely common in the study population, with nearly 50% and more than 11% of older adults receiving greater than or equal to 5 or greater than or equal to 10 drugs, respectively. These data are in accordance with findings from a former study performed in a population of older adults in the United States (25), and are clinically relevant, as polypharmacy increases the risk of adverse drug reactions and poor health outcomes including falls, hospitalization, and death (26–28). Interestingly, the prevalence of polypharmacy was lower in individuals aged 85 years or more than in those 75–84 years of age, a finding that may reflect a more careful approach to pharmacological treatment of the oldest old. Indeed, the coexistence of clinical complexity and limited life expectancy, along with the lack of evidence on drug effectiveness from clinical trials in very old persons, does not provide physicians with knowledge on outcomes associated with an aggressive pharmacological treatment (29–31).

We also found a low prevalence of statins use in diabetics, and poor adherence as well, particularly in the oldest subgroup. This prevalence was exceedingly higher than that described in previous studies with largely different samples enrolled in different settings (19,32–35). Such a difference might be due to the fact that previous analyses of limited and selected samples in observational studies may have resulted in overoptimistic estimates of these phenomena, which may become more common when assessed in a general, ‘real-word’ population. Compared with the above-described indicators, prescribing cascade and potential drug–drug interactions had a substantially lower prevalence: 0.2% of the study population received concomitant dispensing of antipsychotic and anti-Parkinson drugs, 0.2% of warfarin, nonsteroidal anti-inflammatory drugs or cyclooxygenase-2 inhibitors and aspirin or antiplatelets, 0.3% of two or more drugs prolonging the QT interval, and 0.7% of angiotensin-converting enzyme inhibitors or angiotensin receptor blockers and aldosterone antagonists and nonsteroidal anti-inflammatory drugs or cyclooxygenase-2 inhibitors. However, these indicators describe potentially high risk combinations, and when
results are translated into absolute numbers, they raise relevant concerns. For example, more than 35,000 older adults were considered to be at risk of potentially life-threatening arrhythmias because of drugs known to prolong the QT interval. This represents an impressive finding, suggesting the urgent need of interventions targeted at improving the use of these drugs in older persons. Similarly, indicators assessing drugs to be avoided, despite a low prevalence, identified prescription patterns that may increase the risk of adverse drug reactions with potentially severe health consequences. For example, digoxin was shown to cause about 8% of all drug-related hospital admissions in Italy and it had the third highest hospitalization rate for adverse drug events in the United States (36,37). Chlorpropamide and glybenclamide have the highest risk of hypoglycemia among sulfonylureas and they were associated with a significant higher risk of mortality when compared with other oral hypoglycemic agents (38). Finally, short-acting nifedipine and doxazosin were shown to substantially increase the rate of cardiovascular events as compared with other antihypertensive agents (39,40).

OsMed database includes data on 94% of older individuals in Italy, and no drug data was recorded for 6% of them. This finding may be due to the fact that these individuals did not receive any drugs reimbursed by the NHS during the study year. However, our overall findings are similar to those from a survey conducted in the United States, which found that 91% of men and 94% of women aged 65 or older were receiving drug prescriptions (25).

This study has several limitations to be acknowledged. First, the OsMed database includes only prescriptions that were dispensed by pharmacies and, therefore, prescriptions that were not filled were not recorded. This may have led to overestimate undertreatment, even though marginally. Second, quality indicators developed from the OsMed database only included agents reimbursed by the Italian NHS and for this reason did not assess important areas of suboptimal prescribing (ie, benzodiazepines with long half-life or drugs with anticholinergic properties, which are not reimbursed by the Italian NHS). In addition, the prevalence of the quality indicator on polypharmacy might be underestimated due to the exclusion of drugs not reimbursed by the NHS. Third, the proposed quality indicators provide an overall measure of prescribing performance, which can be used in epidemiological studies to assess areas of poor quality of prescribing, but they are not meant to be used as a tool to assess individual patient prescribing appropriateness and safety. Finally, we examined prevalence of quality indicators in the Italian older population and these data cannot be generalized to populations from other countries because prescribing patterns may be influenced by differences in national drug formularies or local policies.

In summary, this study proposes a set of indicators assessing the quality of drug prescribing and, for the first time, explicit criteria of drug prescribing quality have been evaluated at a nationwide level with more than 60 million general population and more than 12 million individuals aged 65 years and older. This approach highlighted the huge dimension of suboptimal drug prescribing in older adults, a finding demanding the urgent implementation of national educational programs, targeted at increasing an appropriate use of medicines. We believe that this synthetic set of indicators, tested on a large national database such as the OsMed, provides a valuable tool to assess longitudinally the impact of such educational programs on the appropriateness of drug prescription in older persons.

**Supplementary Material**

Supplementary material can be found at: [http://biomedgerontology.oxfordjournals.org/](http://biomedgerontology.oxfordjournals.org/)

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**Conflict of Interest**

None.

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