

# Inappropriate Drug Prescribing in Home-Dwelling, Elderly Patients

## A Population-Based Survey

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**Background:** In 1997, a US expert panel developed explicit criteria on potentially inappropriate drugs for the general elderly population.

**Objective:** To investigate the proportion of inappropriate medications among home-dwelling, elderly patients in Helsinki, Finland, between November 1, 1998, and March 31, 1999.

**Methods:** A cross-sectional mail survey was sent to a random sample of 3921 elderly urban residents aged 75, 80, 85, 90, and 95 years. Of these, 3219 were home dwellers.

**Main Outcomes Measures:** Prevalence of potentially inappropriate drugs and prevalence of drugs considered inappropriate related to 15 common medical conditions according to recommendations given by the expert panel in 1997.

**Results:** The response rate was 78%. Of the respondents, 12.5%, 1.3%, and 0.2% were taking at least 1, 2, or 3 inappropriate drugs, respectively. The most preva-

lent inappropriate drugs were dipyridamole (3.6%), long-acting benzodiazepines (2.6%), amitriptyline hydrochloride (1.6%), ergot mesyloids (1.6%), muscle relaxants (1.2%), and meprobamate (1.1%). Use of medications considered inappropriate with certain medical conditions was higher: 27.2% of patients with chronic obstructive pulmonary disease were taking  $\beta$ -blockers and 19.3% used sedatives. Of diabetic individuals taking oral hypoglycemics or insulin, 32.5% were taking a concomitant  $\beta$ -blocker. Of those with a peripheral vascular disease, 37.9% were taking  $\beta$ -blockers. However, two thirds of all these patient groups had concomitant coronary heart disease.

**Conclusions:** Compared with previous surveys, the use of inappropriate medications in our home-dwelling, elderly population is conspicuously low. In contrast, use of certain drugs considered inappropriate with different medical conditions was relatively high. However, the inappropriateness of the latter treatments may be questioned in individual patients.

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**M**ULTIPLE DRUG use is common in elderly patients because of an increase in the number of medical conditions as one ages.<sup>1,2</sup> Multiple drug use increases the risk of drug interaction, adverse outcomes,<sup>3-5</sup> and noncompliance as well as increasing the cost of care.<sup>6</sup> Polypharmacy and use of inappropriate drugs are associated with age, multiple diseases, recent hospitalization, female sex, depression, and the number of physicians prescribing drugs to elderly patients.<sup>1,3,7,8</sup> Iatrogenic syndromes associated with inappropriate drug use have accounted for a large number of hospital admissions in elderly patients.<sup>9-13</sup>

Since 1991, attention has been focused on the quality of prescribing drugs for frail, elderly patients after an expert panel using Delphi techniques gave rec-

ommendations on appropriate drug prescribing.<sup>14</sup> Investigations of elderly populations according to the 1991 criteria have suggested that inappropriate drug prescribing is surprisingly common among elderly patients in the community,<sup>15,16</sup> outpatient departments,<sup>17</sup> board and care facilities,<sup>18</sup> and nursing homes.<sup>19,20</sup> Most of these studies did not apply the full set of

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criteria but modified them by omitting, for example, antihypertensive drugs or ergot mesyloids and cerebral vasodilators from the list.<sup>21</sup> Furthermore, application of these criteria to general elderly populations has been criticized.<sup>22</sup> Consequently, new criteria were developed by a second expert panel for general elderly populations and

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## PATIENTS AND METHODS

In 1999, we obtained a random sample of birth cohorts aged 75, 80, and 85 years ( $n=1000$  in each) and all 90-year-olds ( $n=774$ ) and 95-year-olds ( $n=147$ ) from the Helsinki city area. This area has a population of approximately 500 000 inhabitants, with 13.5% of these 65 years or older. All Finnish citizens are covered by the public health care system, but a private system is also available. Thus, hundreds of physicians are involved in prescribing medication for this population. However, because of the restricted number of medical schools and comprehensive national guidelines, the practice of individual physicians is considered uniform. The random sampling was performed and addresses provided by the Central Population Register of Finland; 82% of the sample were home dwellers.

Mailed questionnaires were sent between November 1, 1998, and March 31, 1999, and questionnaires were resent once to nonresponders. Those individuals who provided incomplete answers were contacted by the study nurse via telephone. Participants were asked to list prescription and nonprescription drugs, vitamins, and natural products used. The questionnaire also contained questions on symptoms and diseases as well as demographic characteristics, functioning, quality of life, and social aspects of the participants. Inappropriate drugs were coded according to the classes proposed by an expert committee.<sup>22</sup> We also coded drugs considered inappropriate with certain diagnoses and symptoms. The study was approved by the local ethics committee.

Questionnaires were coded using the Microsoft ACCESS software (Microsoft Inc, Redmond, Wash) and analyzed with the NCSS (Number Cruncher Statistical System) for Windows statistical program (NCSS, Kaysville, Utah). Drug use was reported as percentages and the proportions were compared with  $\chi^2$  tests. Confidence intervals (CIs) were calculated as previously described.<sup>26</sup>  $P \leq .05$  was considered statistically significant.

elderly persons with certain medical conditions.<sup>22</sup> The updated criteria extended the 1991 criteria by adding gastrointestinal antispasmodics, antihistamines with anticholinergic properties, disopyramide, meperidine hydrochloride, and ticlopidine hydrochloride to the list of inappropriate medications and by including 35 criteria that defined potentially inappropriate medication use in older persons known to have any of 15 common medical conditions. One study has applied the latest criteria to a selected elderly population (clients enrolled in a Medicaid-supported managed care plan in the United States) and found that 39.7% were using at least 1 inappropriate drug from the general criteria.<sup>23</sup> Moreover, 2 studies<sup>24,25</sup> have investigated inappropriate medications in general populations in which 22% to 27% of individuals were found to be using contraindicated drugs. However, these studies did not apply the criteria developed for elderly persons with certain diseases. In addition, they

applied the criteria from 1997 to population data derived from a time preceding development of these criteria.

Evidence concerning the efficacy and safety of drugs changes rapidly. Similarly, the prevalence of drug use at the population level evolves with time. Thus, the use of inappropriate drugs should be evaluated regularly to give feedback to clinicians. As far as we know, no studies exist that have applied the criteria of inappropriate drug use to elderly populations outside the United States and Canada.

The aim of our study was to use the explicit criteria developed by the expert panel in 1997 to evaluate how the guidelines for inappropriate medications had been applied to an urban, home-dwelling, elderly population at the end of the 1990s. We also wanted to investigate whether factors that previously have been discovered to be associated with the use of inappropriate drugs determine drug use in an elderly Finnish population.

## RESULTS

The response rate among home-dwelling, elderly patients was 78%. This rate was calculated by excluding those who had died before the questionnaire was mailed (5.1%) and those permanently institutionalized (10.4%).

Although 79.9% of women and 75.7% of men had some regular medication, 12.5% (95% CI, 11.2%-13.8%) used at least 1 inappropriate drug routinely (**Table 1** and **Table 2**). Of these, the most commonly used were dipyridamole (3.6%), long-acting benzodiazepines (2.6%), amitriptyline hydrochloride (1.6%), ergot mesyloids (1.6%), muscle relaxants (1.2%), and meprobamate (1.1%). Use of other inappropriate drugs was uncommon (Table 2). No statistical differences were found between sexes.

The use of medications that are considered inappropriate with the 15 common medical conditions was common (**Table 3**). A  $\beta$ -blocker was used by 32.5% of diabetic patients taking oral hypoglycemics or insulin, 37.9% of patients with peripheral vascular disease, 21.4% of patients with asthma, and 27.2% of those with chronic obstructive pulmonary disease (COPD). However, two thirds of these patients had concomitant coronary artery disease. In addition, 19.3% of patients with COPD were using a sedative, and 1 in 10 with a history of gastroduodenal ulcer was taking a nonsteroidal anti-inflammatory drug or high-dose aspirin. However, one third of the latter individuals had a concomitant gastroprotective drug (histamine<sub>2</sub> blocker, proton pump inhibitor, or misoprostol). One in 5 patients with constipation requiring laxatives was using an anticholinergic or narcotic drug or a tricyclic antidepressant.

The population was divided into groups according to the characteristics known from previous studies<sup>1,3,7,8</sup> to be associated with the use of inappropriate drugs, and the subgroups were compared accordingly (**Table 4**). Analyses showed that older age (80 years or older), multiple use of medications, depressive feelings, and poor subjective health were risk factors for the use of inappropriate drugs.

In addition, we tested how elderly individuals with certain diagnoses taking essential drugs for their disease

**Table 1. Demographic Characteristics of the Study Population**

Characteristic	Subjects, % (N = 2511)
Age, y	
75	28.8
80	28.2
85	24.5
90	16.2
95	2.4
Female	71.0
Widowed	46.1
Living alone	60.7
Primary school education or less	53.6
Medication	
Regular medication	78.7
Cardiovascular medication	66.7
Physical functioning*	
Able to go outdoors daily	77.3
Needs help daily	16.3
Medical conditions†	
Coronary heart disease	27.8
Diabetes	11.4
Hypertension	46.0
Stroke or transient ischemic attack	13.9
Memory problems	18.5
Feeling depressed‡	4.5
Poor subjective health§	21.7

\*Self-report from the following questions: Do you go outdoors daily? Do you need another person's help daily?

†Self-reported medical conditions.

‡Self-report from the following alternatives: feeling depressed never, sometimes, or daily; those reporting feeling depressed daily were defined as feeling depressed.

§Self-report from the following alternatives: feeling healthy, fairly healthy, ill, or very ill; those answering ill or very ill were defined as having poor subjective health.

differ from those with same diagnoses but not taking essential drugs in their concomitant use of inappropriate drugs. However, those patients with coronary heart disease or previous myocardial infarction taking both aspirin and a  $\beta$ -blocker<sup>27</sup> (n=277) did not differ in their use of inappropriate drugs (14.4%) from other patients (15.4%) with the same diagnoses (n=449) but not taking aspirin or a  $\beta$ -blocker. In addition, patients with chronic heart failure using angiotensin-converting enzyme inhibitors<sup>28</sup> (n=162) did not differ in their use of inappropriate drugs (16.0%) from other patients (16.3%) with chronic heart failure who were not using angiotensin-converting enzyme inhibitors (n=569).

### COMMENT

In the Finnish, urban, elderly population, the rate of use of at least 1 inappropriate drug was 12.5%, which is markedly less than the rates previously reported from the United States.<sup>15,16,24,25</sup> To our knowledge, this is the first study to apply the additional criteria, which define potentially inappropriate medications in association with 15 common medical conditions in elderly patients.<sup>22</sup> Our findings show that the use of these contraindicated drugs is common, especially the use of  $\beta$ -blockers in conjunction with diabetes, asthma, COPD, and peripheral vascular disease.

**Table 2. Prevalence of Elderly Patients Using Drugs Considered Potentially Inappropriate for the General Elderly Population<sup>22\*</sup>**

Type of Medication	Severe Potential Adverse Effects	Patients Using Drug, % (95% CI)
Use of any general inappropriate drugs	...	12.5 (11.2-13.8)
Propoxyphene and combination products	No	0.5 (0.3-0.8)
Indomethacin	No	0.4 (0.2-0.7)
Phenylbutazone†	No	...
Pentazocine†	Yes	...
Trimethobenzamide†	No	...
Muscle relaxants and antispasmodics (methocarbamol, carisoprodol, oxybutynin, chlorzoxazone,† metaxalone,† cyclobenzaprine†)	No	1.2 (0.8-1.7)
Amitriptylin, chlordiazepoxide-amitriptylin	Yes	1.6 (1.1-2.2)
Doxepin	Yes	0.4 (0.2-0.8)
Meprobamate	Yes	1.1 (0.7-1.6)
Long-acting benzodiazepines (chlordiazepoxide, diazepam, flurazepam†)	Yes	2.6 (2.0-3.3)
Disopyramide (without artificial heart valves)	Yes	0.3 (0.1-0.6)
Dipyridamole	No	3.6 (2.9-4.4)
Methyl dopa, methyl dopa-hydrochlorothiazide†	Yes	0.04 (0.006-0.2)
Reserpine, reserpine-hydrochlorothiazide	No	0.08 (0.006-0.3)
Chlorpropamide†	Yes	...
Gastrointestinal antispasmodics (dicyclomine,† hyoscyamine, propantheline,† belladonna alkaloids, clidinium-chlordiazepoxide)	Yes	0.1 (0.03-0.3)
Antihistamines with anticholinergic properties (chlorpheniramine, diphenhydramine, hydroxyzine, cyproheptadine,† promethazine,† tripelemamine, dexchlorpheniramine)	No	0.7 (0.4-1.1)
Diphenhydramine	No	...
Ergot mesyloids or cyclandelate	No	1.6 (1.2-2.2)
Barbiturates except phenobarbital	Yes	0.04 (0.006-0.2)
Meperidine†	Yes	...
Ticlopidine	Yes	...

\*N = 2511. CI indicates confidence interval; ellipses, not applicable.

†Not available in Finland.

Findings from many former studies<sup>16,24,25</sup> of community-dwelling, elderly patients have shown that 20% to 27% use inappropriate drugs. However, the proportion of these patients depends on the criteria used, and with a more conservative application of criteria, the proportion is reduced to 14%.<sup>15</sup> Among frail, elderly patients and those in nursing homes, the use may be as high as 40%,<sup>19,23</sup> but again, lower figures have been found when only a portion of the inappropriate drugs were studied.<sup>20</sup>

Of the most commonly used inappropriate drugs, dipyridamole, long-acting benzodiazepines, and amitriptyline have frequently appeared in previous studies,<sup>15-20,23-25</sup> but their use was clearly less frequent in our study. However, some of the most commonly used inappropriate drugs in the United States (eg, chlorpropamide) are not available in Finland. In fact, the national drug policy may have a great impact on inappropriate drug use. Drugs such as phenylbutazone, pentazocine, trimethobenzamide hy-

**Table 3. Prevalence of Elderly Patients Using Drugs Considered Inappropriate in Relation to Common Medical Conditions<sup>22\*</sup>**

Type of Medication (n/N)	Severe Potential Adverse Effects	Those Having the Disease or Symptoms Using Drug, % (95% CI)
Heart failure		
With disopyramide (1/731)	Yes	0.1 (0.006-0.7)
With drugs with high sodium content (0/731)	No	...
Diabetes (oral hypoglycemics or insulin)		
With $\beta$ -blockers (54/166)	No	32.5 (25.4-39.7)
Hypertension with diet pills or amphetamines	Yes	...
Chronic obstructive pulmonary disease		
With $\beta$ -blockers (82/301)	Yes	27.2 (22.2-32.3)
With sedatives (62/301)	Yes	19.3 (16.0-25.2)
Asthma with $\beta$ -blockers (24/112)	Yes	21.4 (13.8-29.0)
Ulcers		
With NSAIDs or aspirin (>325 mg) (37/342)	Yes	10.8 (7.5-14.1)
With potassium supplements (18/342)	No	5.3 (3.1-8.2)
Epilepsy or seizures with clozapine, chlorpromazine, thioridazine, or chlorprothixene (1/23)	No	4.3 (0.1-22.0)
Peripheral vascular disease and peroneal muscle pain while walking (daily)		
With $\beta$ -blockers (61/161)	Yes	37.9 (30.3-45.4)
With metoclopramide†	Yes	...
Anticoagulant therapy with aspirin, NSAIDs, dipyridamole, or ticlopidine hydrochloride (9/144)	Yes	6.3 (2.9-11.5)
Incontinence with $\alpha$ -blockers (5/264)	No	1.9 (0.6-4.4)
Constipation		
With anticholinergic drugs (5/104)	No	4.8 (1.6-10.9)
With narcotic drugs (12/104)	No	11.5 (5.4-17.7)
With tricyclic antidepressants (8/104)	Yes	7.7 (3.4-14.6)
Insomnia with decongestants, theophylline, desipramine hydrochloride, SSRIs, methylphenidate hydrochloride, MAOIs, or $\beta$ -agonists (43/250)	No	17.2 (12.5-21.9)

\*n Indicates number of participants using inappropriate drugs; N, number of participants having the particular medical condition; CI, confidence interval; ellipses, no users; NSAIDs, nonsteroidal anti-inflammatory drugs; SSRIs, selective serotonin reuptake inhibitors; and MAOIs, monoamine oxidase inhibitors.

†Metoclopramide may worsen peripheral arterial blood flow and precipitate claudication.<sup>22</sup>

drochloride, chlorpropamide, and meperidine hydrochloride are no longer available in Finland. In addition, ticlopidine hydrochloride has been replaced by clopidogrel as a substitute for aspirin or after coronary stenting. Prescribing diphenhydramine hydrochloride is difficult because it is only available in a combination and a separate prescription is needed for each package.

On the other hand, because no evidence-based treatments exist for many common medical conditions, such as leg cramps or vertigo, available symptomatic drugs are used regardless of their effectiveness. Accordingly, use of meprobamate derives from only one preparation containing meprobamate and quinine hydrochloride for leg cramps. The use of long-acting benzodiazepines is in-

**Table 4. Rate of Inappropriate Medication Use in Different Patient Subgroups\***

Characteristic	Those Using Inappropriate Medications, % (95% CI)	P Value for Comparison ( $\chi^2$ Test)
Sex		
Female	13.0 (11.4-14.6)	.24
Male	11.3 (9.0-13.6)	
Age, y		
75	8.3 (6.4-10.6)	.002
80	14.0 (11.5-16.6)	
85	13.9 (11.1-16.6)	
90	15.2 (11.7-18.7)	
95	13.3 (5.9-24.6)	
Education		
$\leq$ Primary school	12.2 (10.4-14.0)	.53
$\geq$ Secondary school	13.0 (11.1-15.0)	
No. of medications		
<4	5.5 (4.4-6.8)	<.001
4-6	18.1 (13.0-23.3)	
>6	30.5 (26.0-35.0)	
Feeling depressed†		
Never	10.2 (8.6-11.8)	<.001
Sometimes	15.6 (12.9-18.4)	
Daily	24.8 (16.8-32.7)	
Subjective health‡		
Healthy or fairly healthy	10.4 (9.0-11.8)	<.001
Ill or very ill	21.1 (17.7-24.5)	

\*CI indicates confidence interval.

†Self-report from the following alternatives: feeling depressed never, sometimes, or daily.

‡Self-report from the following alternatives: feeling healthy, fairly healthy, ill, or very ill.

creased because a popular combination preparation for vertigo contains small doses of diazepam and cyclizine hydrochloride. Moreover, the higher price of some new medications compared with older ones may have an impact. For example, selective serotonin reuptake inhibitors or tetracyclic antidepressants are 3 to 10 times more expensive than tricyclics. If a depressed, elderly person cannot afford a selective serotonin reuptake inhibitor, the physician may elect to prescribe the second best choice, even with the risk of adverse effects. In addition, since tricyclic agents are evidence-based treatment for neuropathic pain,<sup>29,30</sup> a significant proportion of their use may derive from this indication. Thus, inappropriate use is not always easy to define explicitly, and individual decisions may be justified.

The use of dipyridamole has increased only recently in Finland. At the beginning of the 1990s, results from a meta-analysis<sup>31</sup> indicated that dipyridamole had no benefit over aspirin alone in the prevention of stroke. However, the European Stroke Prevention Study 2,<sup>32</sup> a randomized study with more than 6600 patients and 4 treatment arms (aspirin alone, dipyridamole alone, aspirin plus dipyridamole, placebo), showed that aspirin alone and dipyridamole alone were more effective than placebo in reducing the risk of stroke in secondary prevention. Most effective in this respect was a combination of aspirin and dipyridamole. In our study, 46 (51%) of 90 dipyridamole users reported having had a previous stroke or transient ischemic attack, with 38 (83%) of these 46 users taking

the most effective regimen according to the European Stroke Prevention Study 2 (ie, the combination of dipyridamole and aspirin). Thus, about half of the users may be taking dipyridamole inappropriately.

A large proportion of inappropriate drug use is derived from patients with the following medical conditions taking  $\beta$ -blockers: diabetes (only with oral hypoglycemics or with insulin), peripheral vascular disease, asthma, or COPD. However, comorbidity of coronary heart disease is common in patients with diabetes and peripheral vascular disease. In our cohort, 68.5% of patients with type 2 diabetes mellitus and 70.5% of those with peripheral vascular disease who were taking a  $\beta$ -blocker had a concomitant coronary artery disease. Because  $\beta$ -blockers improve prognosis of diabetic patients with coronary artery disease<sup>33</sup> or hypertension,<sup>34</sup> physicians may justify their decisions if they follow up the patients and possible adverse effects properly. The same applies to patients with asthma and COPD, among whom coronary artery disease was also found to be very common (58.3% and 68.3%, respectively). Fortunately, most  $\beta$ -blockers were  $\beta_1$ -selective agents. Of asthmatic patients using  $\beta$ -blockers, 29% were taking superselective agents (bisoprolol fumarate, celiprolol) and an additional 63% were taking  $\beta_1$ -selective agents. For patients with COPD using  $\beta$ -blockers, the respective figures were 30% and 46%. These findings suggest that physicians generally are aware of the possible harms of  $\beta$ -blockers on respiratory function and make their choices accordingly.

However, a closer look at, for example, patients with peripheral vascular disease but without coronary artery disease who were taking  $\beta$ -blockers revealed other ambiguities in drug use: 7 of 18 used another inappropriate drug (tricyclics, sedatives, dipyridamole, indomethacin) and an additional 4 of 18 used weak opioids. This may suggest that the latter medications were used to counteract the adverse effects of  $\beta$ -blockers.

On the other hand, older individuals are at risk of underuse of essential medications.<sup>27,35</sup> We hypothesized that there might be an inverse relationship between prescribing evidence-based drugs for certain diagnoses in a patient and prescribing inappropriate medications in the same patient. However, this was not the case: the use of evidence-based drugs did not protect the patient from using inappropriate medications, at least not among patients with coronary heart disease or heart failure.

Our study contained several possible limitations. First, mailed surveys may not be a reliable method when questioning elderly people about drug use and actual daily doses used. Nonetheless, the proportion using, for example, analgesics was very similar to the figures based on another survey of health behavior among Finnish, elderly patients in 1997.<sup>36</sup> Second, all the Beers criteria could not be used with our participants because of the cross-sectional nature of the study. Some criteria are based on data of the length of use of medications (corticosteroids), others on daily doses (short half-life benzodiazepines, digoxin, iron supplements). The latter data were not considered sufficiently reliable.

Third, one may also question the reliability of self-report on diagnoses. However, the prevalences of all major diagnoses corresponded well to the epidemiologic Hel-

sinki Aging Study, in which a random sample of the same age groups from the same area was assessed carefully and individually for diseases.<sup>37</sup> No other population data are currently available in Finland for these age groups. We could not apply some of the Beers criteria since definitions of certain medical conditions could not be formulated reliably in our survey (benign prostate hyperplasia, arrhythmias, syncope, and falls). On the other hand, definitions of cardiovascular conditions were adhered to strictly; for example, peripheral vascular disease was defined as a self-report of diagnosis plus daily symptoms in peroneal muscles while walking. Applying the criteria in a conservative manner may underestimate the actual use of inappropriate medications. However, to the best of our knowledge, we have included more of the Beers criteria than any previous study.

Weighing the potential benefits and harms against individual patients may lead to prescribing decisions that are inappropriate if inflexible and explicit criteria are used. Older people are a heterogeneous group, and choice of treatment should depend on assessing individual predictors of outcome. A closer look at the diagnoses and drug indications reveals the difficulty in applying inflexible criteria. In addition, the evidence for potential benefits and harms changes rapidly, and thus, the criteria should be reviewed regularly. However, truly problematic use of inappropriate drugs tends to occur among individuals who use criteria-based inappropriate drugs. Thus, the criteria might be used to flag persons at risk rather than to impose explicit and inflexible standards for appropriate prescribing.

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