Questionable prescribing for elderly patients in Quebec

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Objective: To estimate the prevalence of questionable and rational high-risk prescribing among elderly people of the three drug groups most commonly implicated in drug-related illness: cardiovascular drugs, psychotropic drugs and nonsteroidal anti-inflammatory drugs (NSAIDs).
Design: Retrospective prevalence study; all prescription and billing records for the period Jan. 1 to Dec. 31, 1990, for the study sample were retrieved from the relevant provincial databases of the Régie de l'assurance-maladie du Québec.
Setting: Quebec.
Participants: Regionally stratified random sample of 63 268 elderly medicare registrants who made at least one visit to a physician in 1990 and were not living in a health care institution for the entire year.
Main outcome measure: Prescription information was examined for three types of high-risk prescribing: rational and questionable drug combinations, excessive treatment duration and drugs relatively contraindicated for use in elderly people.
Results: Overall, 52.6% of the patients experienced one or more events of high-risk prescribing, and 45.6% experienced at least one that was questionable. High-risk prescribing was most prevalent for psychotropic drugs, and questionable prescribing was more frequent than rational prescribing in this drug group. An estimated 30.8% of the total elderly population in Quebec received benzodiazepines for more than 30 consecutive days, 12.9% received a long-acting benzodiazepine, and 13.0% received a questionable high-risk psychotropic drug combination. The prevalence of high-risk prescribing was higher among the women than among the men and increased with age until 75 to 84 years. There were significant unexplained differences between regions in the regional prevalence of high-risk prescribing, particularly of psychotropic drugs.
Conclusion: The prevalence of questionable high-risk prescribing, especially of psychotropic drugs, is substantial among elderly people. This may be a potentially important and avoidable risk factor for drug-related illness in elderly people.

Objectif : Évaluer la prévalence des ordonnances à risque élevé douteuses et rationnelles, chez les aînés, des trois groupes de médicaments liés plus souvent aux maladies d'origine médicamenteuse : médicaments cardiovasculaires, psychotropes et anti-inflammatoires non stéroïdiens (AINS).

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Conception : Étude de prévalence rétrospective; tous les dossiers d'ordonnances et de facturation de la période du 1er janvier au 31 décembre 1990 de l'échantillon visé par l'étude ont été extraits des bases de données provinciales pertinentes de la Régie de l'assurance-maladie du Québec.
Contexte : Québec.
Participants : Échantillon aléatoire stratifié régionalement de 63 268 aînés inscrits à l'assurance-maladie qui ont consulté au moins une fois un médecin en 1990 et n'ont pas vécu toute l'année dans un établissement de soins de santé.
Principales mesures de résultats : On a étudié l'information sur les ordonnances pour en extraire trois types d'ordonnances à risque élevé : combinaisons de médicaments rationnelles et douteuses, durée excessive du traitement et médicaments relativement contre-indiqués chez les aînés.
Résultats : Dans l'ensemble, 52,6 % des patients ont obtenu une ou plusieurs ordonnances à risque élevé et 45,6 % en ont obtenu au moins une qui était douteuse. Les ordonnances à risque élevé ont été les plus fréquentes dans le cas des psychotropes et les ordonnances douteuses ont été plus fréquentes que les ordonnances rationnelles dans cette catégorie de médicaments. On estime que 30,8 % des aînés du Québec ont reçu des benzodiazépines pendant plus de 30 jours consécutifs, 12,9 %, des benzodiazépines à effet prolongé et 13,0 %, une combinaison douteuse de psychotropes à risque élevé. La prévalence des ordonnances à risque élevé était plus élevée chez les femmes que chez les hommes et a augmenté avec l'âge jusqu'à 75 à 84 ans. On a constaté d'importants écarts inexpliqués entre les régions au niveau de la prévalence régionale des ordonnances à risque élevé, et particulièrement des ordonnances de psychotropes.
Conclusion : La prévalence des ordonnances à risque élevé douteuses, particulièrement de psychotropes, est importante chez les aînés. Il pourrait s'agir d'un facteur de risque important et évitable de maladies d'origine médicamenteuse chez les aînés.

Health problems affecting elderly people are of increasing concern as the proportion of people 65 years of age and older increases in the population.[1] Of elderly people 78% have at least one chronic disease, and 30% have three or more.[2] Although the frequency of use of ambulatory health care services among elderly patients is similar to that among younger people,[3,4] the former group accounts for a disproportionate amount of prescription drug use.[1,5] For example, in Saskatchewan people 65 years of age and older account for 15% of the patient population but for 41% of all prescriptions.[6] Consistent with these observations, most studies have found that elderly patients are two to three times more likely than younger people to be admitted to hospital because of a drug-related illness.[7]

Drug-related illness is the primary reason for 1% to 5% of medical visits,[8,9] 3% to 23% of hospital admissions[7,10,11] and 1 in 1000 deaths.[12] The excess of drug-related illness in the elderly population has been attributed to age-related changes in drug metabolism and excretion,[13,14] an increased likelihood of multiple health problems, which may require more medication and high-risk combinations of drugs for effective disease control,[7,15] and unintentional misuse of medication because of impaired visual, motor and memory abilities.[16–20] Also, Ferguson[21] suggested that suboptimal prescribing is an important risk factor for drug-related illness among elderly people. She found that the proportion of prescriptions in general practice that were inappropriate was 7% to 14% higher among elderly patients than among middle-aged patients. Generally, these findings are consistent with the literature: 18% to 50% of prescriptions for elderly patients are estimated to be inappropriate.[21–23] Evidence linking inappropriate prescribing to drug-related illness has been provided by Grymonpre and associates,[15] who found that 19% of admissions because of drug-related illness were attributed to inadequate or inappropriate drug therapy.

However, a true understanding of the magnitude of the problem of inappropriate prescribing is limited by two considerations. First, the existing literature bases population estimates on the selected subpopulation of physicians who participate in studies. Second, definitions of inappropriate prescribing have grouped rational high-risk prescriptions of drug combinations with prescriptions whose efficacy in elderly patients would be questionable in all but the rarest of circumstances.

We undertook this study to address these issues. Using information from provincial health care databases we estimated (a) the prevalence of high-risk prescribing of the three groups of drugs most commonly implicated in drug-related illness (cardiovascular drugs,[24–28] psychotropic drugs[29–32] and nonsteroidal anti-inflammatory drugs [NSAIDs][15,24–26,33–36]), (b) the proportion of high-risk prescriptions that were either rational (justified in some disorders because of known therapeutic benefit) or questionable (not justified in elderly patients except in rare circumstances) and (c) the prevalence of high-risk prescriptions by age, sex and health care region.

Methods

We conducted a prevalence survey using data from Jan. 1 to Dec. 31, 1990, for a regionally stratified random sample of elderly patients. Eligible patients were those

who were 65 years of age or older on Jan. 1, 1990, had at least one billing for a physician visit during the study period and were registered as a medicare card holder in Quebec. (As of July 1, 1990, 753 446 Quebec residents 65 years or older were registered for Quebec medicare coverage;[37] this represented 97.7% of the 770 925 Quebec residents in that age group according to 1991 census data.[38] Elderly people who reside outside of the province for more than 183 days in the year are ineligible for Quebec medicare coverage.) A sample of 6040 eligible patients was randomly selected from each of the 12 health care regions in Quebec, the sample being drawn from the database of medicare registrants of the Régie de l'assurance-maladie du Québec (RAMQ). In the two remote regions with fewer than 6040 eligible patients, all eligible patients were included. The total sample was 65 349 patients.

Information about age, sex and region of residence of the patients was retrieved from the RAMQ demographic database. Data on all physician billings (1 107 271) and prescription records (1 919 043) during the study period for patients in the sample were retrieved from the RAMQ prescription and billing databases. Data on billings and prescriptions were linked to each patient using the patient's scrambled medicare number. Patients who were in an institution for all of 1990 were excluded before analysis of the data, because the RAMQ does not record prescription data for these patients. For patients who were in an institution and in the community in 1990, prescribing information was based on the drugs dispensed to them while in the community. The patient's location of care during the study period was determined from the service location code on the physician's billing record. Patients were classified as being in an institution for all of 1990 if all billings were from an inpatient setting. It was assumed that drugs dispensed to patients were taken for the prescribed treatment period. Medication code, treatment duration and the date the drug was dispensed were used to create a matrix of the drugs prescribed per patient for each day in the 1-year follow-up period. Complete information was present on all demographic variables for each patient. Information was missing or invalid for the service location code in 0.01% of the records, for the medication code in 0.63%, for the treatment duration in 0.76% and for the date the prescription was dispensed in 0.39%.

There were sufficient data from the RAMQ prescription records to document three main types of high-risk prescribing: drugs prescribed for an excessive duration (benzodiazepines for more than 30 consecutive days), drugs that were relatively contraindicated for use in elderly patients (long-acting benzodiazepines, phenylbutazone) and drug combinations with a potential risk of interaction. Using a quarterly expert review of drug interactions,[39] we defined a subset of high-risk drug combinations for which there was established evidence of a risk of drug interaction that could result in significant deterioration in patient health or death. On the basis of this review we defined 56 high-risk combinations for cardiovascular drugs, 50 for psychotropic drugs and 14 for NSAIDs (Appendix 1). Computer algorithms were then developed for each drug combination and applied to the matrix of drugs–days constructed for each patient. For each combination assessed, we counted only the first calendar event detected for each patient in the study period.

High-risk drugs and drug combinations were classified as rational or questionable. This classification was based on published data for the categories of excessive duration and contraindicated drugs and on expert review for drug combinations. Benzodiazapine treatment for more than 30 days was defined as questionable because of the absence of an indication in all but 1% to 2%[40,41] of patients with selected psychiatric disorders and because of the problems of habituation, loss of efficacy and disturbance in sleep patterns with prolonged treatment.[42–44] Prescription of long-acting benzodiazepines was defined as questionable because of the increased risk of falls, fractures and confusion among elderly patients using these medications[31,32] and the absence of evidence showing an advantage over short-acting products. Prescription of phenylbutazone was defined as questionable because of the risk of bone-marrow suppression and the availability of suitable alternative drugs for rheumatic disorders in elderly patients.[45]

High-risk drug combinations were independently classified by a review panel of six academically affiliated specialists who would commonly prescribe these drugs (cardiologists, psychiatrists and internists). There was unanimous agreement in classifying drug combinations as rational or questionable for 83% of the cardiovascular drug combinations, 80% of the psychotropic drug combinations and 100% of the NSAID combinations. Disagreements were arbitrated by a clinical pharmacologist (P.J.M.). Eleven of the 56 cardiovascular, 15 of the 50 psychotropic and 3 of the 14 NSAID high-risk drug combinations were classified as questionable (Appendix 1).

We evaluated the frequency of rational and questionable high-risk prescribing by drug category using the first event detected in the study period for each patient. To produce population estimates of high-risk prescribing, we first estimated the expected number of events in each health care region by multiplying age- and sex-specific prevalence rates of high-risk prescribing in each region by the proportion of elderly people in each age and sex group who visited a physician in 1990 in that region.[37] We then summed the expected number of events across regions and divided the figure by the total number of elderly people registered with the RAMQ in 1990. Contingency tables were used to summarize frequency by age, sex and region. Differences in prevalence were evaluated with the χ^2 test for categoric variables and logistic regression analysis for continuous variables (age), the type I error being corrected for multiple comparisons. We obtained age- and sex-standardized prevalence rates of high-risk prescribing by using the Quebec popu-

lation of elderly people in 1990 as the population standard.

Results

The elderly population and the characteristics of the study sample by health care region are displayed in Table 1. The mean age in the study sample was 75.0 (range 65 to 111) years. Consistent with the regional sex distribution among Quebec elderly people,[37] there was a greater proportion of women in the predominantly urban regions than in the remote areas. Of the 65 349 patients 2081 (3.2%), whose mean age was 80 years, were removed from analysis because they were in an acute or chronic care institution for all of 1990. Two thirds of the study sample had received all of their care in 1990 in the community.

For the 63 268 remaining patients the median number of physician visits in 1990 was 8 (range 1 to 475). All but 166 (0.3%) of the patients had received a prescription in 1990; 56.9% of the patients received a prescription for one or more cardiovascular drugs, 56.2% for an NSAID and 48.5% for a psychotropic drug. Two thirds of all prescriptions were for drugs in these three groups, and 80% of the prescriptions were written by general practitioners. The median number of prescriptions per patient was 22; the median was slightly higher for the women than for the men (24 and 18 respectively).

The prevalence of rational and questionable high-risk prescribing is reported in Table 2. Overall, 52.6% of the patients had one or more high-risk prescribing events in 1990, and 45.6% received at least one questionable prescription. A rational high-risk drug combination was prescribed for 26.4% of the patients and a questionable combination for 29.0%. NSAIDs were the most prevalent form of rational drug combination (13.7% of the patients). Questionable prescribing was most common with the psychotropic drugs: 15.6% of the patients had a questionable psychotropic drug combination, 36% received benzodiazepines for more than 30 consecutive days, and 15.4% were prescribed a long-acting benzodiazapine. Only 41 patients (0.1%) had a prescription for phenylbutazone.

The estimated population prevalence of high-risk prescribing among elderly people was lower than that observed in the study sample (Table 2), because 8% to 16% of the elderly people in the 12 health care regions did not visit a physician in 1990, and the region with the largest population of elderly people had the lowest prevalence of high-risk prescribing. On the basis of these population estimates, almost one third of the elderly people in Quebec were exposed to benzodiazapines for more than 30 consecutive days in 1990.

Table 3 lists the most prevalent high-risk drug combinations. For cardiovascular drugs a prescription of two calcium-channel blockers was the most common questionable combination; a prescription of digitalis and furosemide was the most common rational combination. For the psychotropic drugs the most common questionable combination was of two benzodiazepines; the next most common was of a benzodiazapine and a sedative. For NSAIDs the most common questionable combination was of two NSAIDs, and the most common rational combination was of acetylsalicylic acid (ASA) and an NSAID. We assumed in the latter case that the ASA and the NSAID were usually being used for two different in-

Table 1: Population and characteristics of study sample of people 65 years of age and older in Quebec in 1990, by health care region

Health care region (and no.)	Total elderly population	Study sample: Total no.	% in an institution	% in institution and community	% in community	Mean age, yr	% female patients
Bas Saint Laurent–Gaspésie (1)	38 801	6 040	3.9	32.7	63.4	75.4	56.0
Saguenay–Lac Saint Jean (2)	24 604	6 038	2.5	29.9	67.6	74.5	55.8
Québec–Chaudière (3)	108 277	6 040	3.2	29.0	67.8	75.3	59.7
Trois Rivières (4)	56 477	6 038	3.1	30.4	66.5	75.3	58.7
Estrie (5)	32 708	6 038	2.3	34.7	63.0	75.3	59.1
Montréal–Laval (6)	280 932	6 040	2.3	27.8	70.0	75.3	63.1
Outaouais (7)	23 323	6 040	6.7	46.0	47.3	74.7	56.2
Abitibi–Temiscamingue (8)	12 885	6 040	3.1	33.7	63.1	74.7	54.0
Côte Nord (9)	6 040	4 605	2.6	31.0	66.4	74.5	53.6
Nord du Québec (11)	692	351	4.3	33.6	62.1	74.7	48.4
Laurentides–Lanaudière (16)	61 081	6 040	3.1	25.7	71.2	74.6	56.7
Montérégie (26)	107 646	6 039	2.1	26.8	71.1	74.9	59.1
Total	753 446	65 349	3.2 (2 081)	31.6 (20 670)	65.2 (42 598)	75.0	57.5 (37 576)

dications; for example, it was considered rational to prescribe low-dose ASA for cardiovascular prophylaxis and another NSAID for rheumatic disease.

The age-standardized prevalence of high-risk prescribing among the women and men in the study sample is displayed in Table 4. Except for rational combinations of cardiovascular drugs, the female patients were exposed to significantly more high-risk prescriptions than the male patients ($p < 0.001$). This was especially true for the psychotropic drugs: 5% more women than men were exposed to questionable psychotropic combinations, 11% more women than men were exposed to benzodiazepines for more than 30 days, and 3% more women than men were prescribed long-acting benzodiazepines. Differences in high-risk prescribing between the women and men were mainly due to differences in the proportion of women and men prescribed medication in these drug categories. For example, 54.0% of the women received at least one prescription for a psychotropic drug, as compared with 40.4% of the men. Of these patients, 75.6% of the women and 73.4% of the men received benzodiazepines for more than 30 days.

The prevalence of rational and questionable prescribing increased with age until about 75 to 84 years and then diminished. This age-related increase was primarily due to more patients in higher age groups receiving cardiovascular, psychotropic or NSAID drugs. For example, among the women 65 to 69 years of age 56.1% received a cardiovascular drug and 11.1% received a questionable cardiovascular drug combination. The corresponding figures for women 80 to 84 years of age were 66.7% and 13.7%. The most prevalent questionable

Table 2: Prevalence of high-risk prescribing in the study sample and estimated prevalence in the Quebec elderly population, by high-risk prescribing category*

Prescribing category	% of patients in study sample (and 95% confidence interval)	Estimated no. (and %) of elderly people in Quebec
Rational		
Cardiovascular drug combination	9.1 (8.8–9.4)	56 575 (7.9)
Psychotropic drug combination	8.6 (8.3–8.9)	56 317 (7.8)
NSAID combination	13.7 (13.4–14.0)	85 159 (11.8)
Questionable		
Cardiovascular drug combination	11.6 (11.3–11.9)	72 052 (10.0)
Psychotropic drug combination	15.6 (15.2–16.0)	93 343 (13.0)
NSAID combination	7.9 (7.6–8.2)	49 089 (6.8)
Benzodiazepine > 30 d	36.1 (35.6–36.6)	221 892 (30.8)
Long-acting benzodiazepine	15.4 (15.0–15.8)	92 931 (12.9)
Phenylbutazone	0.1 (0.06–0.13)	332 (0.05)

*High-risk prescribing refers to drugs prescribed for an excessive duration (i.e., benzodiazepines for more than 30 consecutive days), drugs that were relatively contraindicated for use in elderly patients (i.e., long-acting benzodiazepines, phenylbutazone) and drug combinations with a potential risk of interaction. Prescribing was rational if it was justified in some disorders because of known therapeutic benefit; it was questionable if use was not justified to achieve effective treatment except in rare circumstances. NSAID = nonsteroidal anti-inflammatory drug.

Table 3: Most prevalent rational and questionable high-risk drug combinations, by drug group*

Rational combination	% of sample	Questionable combination	% of sample
Cardiovascular		Cardiovascular	
Digitalis + furosemide	4.5	Two calcium-channel blockers	3.4
Digitalis + thiazide	2.8	Thiazide + thiazide	2.2
Psychotropic		Psychotropic	
Benzodiazepine + antidepressant†	5.0	Two benzodiazepines	13.9
Benzodiazepine + tranquillizer‡	3	Benzodiazepine + sedative§	1.9
NSAID		NSAID	
ASA + NSAID	6.3	Two NSAIDs	5.3
NSAID + ß-blocker	4.6	ASA + ASA	2.6

*There was agreement in classification for all drug combinations except the questionable psychotropic combinations, for which 17% of the reviewers felt that they were rational. ASA = acetylsalicylic acid.
†Antidepressant includes amitriptyline, amoxapine, clomipramine, desipramine, doxepin, fluoxetine, imipramine, isocarboxazid, maprotiline, nortriptyline, phenelzine, protriptyline, tranylcypromine, trazodone and trimipramine.
‡Tranquillizer includes chlorpromazine, chlorprothixene, flupenthixol, fluphenazine, fluspirilene, haloperidol, loxapine, mesoridazine, methotrimeprazine, pericyazine, perphenazine, pimozide, pipotiazine, prochlorperazine, promazine, thiopropazate, thioproperazine, thioridazine, thiothixene and trifluoperazine.
§Sedative includes chloral hydrate, hydroxyzine, meprobamate and promethazine.

prescription in all age groups was of psychotropic drugs, and the least common was of NSAIDs. Questionable prescribing of psychotropic drugs was most common among the patients aged 75 to 79: 43.9% of the patients in this age group received benzodiazapines for more than 30 consecutive days, 19.2% received a questionable psychotropic drug combination, and 17.6% received a prescription for a long-acting benzodiazapine.

Table 5 shows the regional prevalence of high-risk prescribing. The 351 patients eligible for inclusion in the remote region of Nord du Québec experienced the lowest prevalence of high-risk prescribing in all drug categories. In the remaining 11 regions, there were modest but significant differences in the rational high-risk combinations ($p < 0.001$). Rational cardiovascular drug combinations were most common in the southwestern regions of Quebec, and rational psychotropic combinations were most common in southeastern Quebec. Among the questionable prescriptions, there were small differences between the regions in the prevalence of prescriptions of cardiovascular drugs and NSAIDs. The largest differences between regions (excluding Nord du Québec) were for questionable psychotropic drug prescribing. Regional differences of up to 5% were observed for psy-

Table 4: Age-standardized rational and questionable high-risk prescribing, by sex and prescribing category*

Prescribing category	% of women	% of women prescribed a drug in respective group	% of men	% of men prescribed a drug in respective group
Rational				
Cardiovascular drug combination	8.9	15.4	8.7	16.9
Psychotropic drug combination	10.5†	18.8†	6.7	16.1
NSAID combination	15.2†	26.0†	12.2	22.1
Questionable				
Cardiovascular drug combination	13.1	21.7†	10.0	19.8
Psychotropic drug combination	18.0†	32.6	13.1	31.8
NSAID combination	8.5†	14.5	7.4	13.5
Benzodiazepine > 30 d	41.7†	75.6†	30.2	73.4
Long-acting benzodiazepine	17.0†	33.9	14.1	33.9
Phenylbutazone	0.05	0.09	0.08	0.02

*Among the women 61.1% were dispensed a cardiovascular drug, 54.0% were dispensed a psychotropic drug, and 57.5% were dispensed an NSAID; the corresponding figures among the men were 50.7%, 40.4% and 52.6%. The second column for each sex represents the prevalence among those dispensed at least one drug in the respective drug group.
†$p < 0.001$.

Table 5: Age- and sex-standardized rational and questionable high-risk prescribing, by health care region* and prescribing category

	Health care region; % of patients											
	Southeastern					Southcentral		Southwestern				North
Prescribing category	1	2	3	4	9	5	6	7	8	16	26	11
Rational												
Cardiovascular drug combination	7.9	8.2	8.2	8.6	7.8	8.0	9.1	8.6	9.2	9.3	9.2	0.5
Psychotropic drug combination†	9.4	9.7	10.7	9.5	6.7	8.1	7.9	8.7	7.0	8.8	8.2	1.1
NSAID combination†	13.0	14.5	12.9	12.5	15.1	12.5	12.6	14.8	13.4	14.3	14.1	1.1
Questionable												
Cardiovascular drug combination‡	11.4	11.4	11.1	10.0	13.6	10.3	11.3	11.4	12.6	11.6	11.0	1.0
Psychotropic drug combination†	17.9	17.3	17.3	16.2	16.8	15.2	12.3	14.9	15.1	15.1	13.1	1.2
NSAID combination†	8.6	7.5	7.3	6.7	8.3	6.9	7.6	8.3	9.4	7.6	7.8	1.0
Benzodiazepine > 30 d†	40.7	37.9	39.4	39.4	36.7	35.1	30.4	33.1	34.7	35.5	32.4	3.3
Long-acting benzodiazepine†	16.8	16.8	18.1	15.9	16.7	15.8	12.2	15.3	14.0	14.6	13.2	1.4
Phenylbutazone	0.02	0.1	0.09	0.12	0	0.07	0.02	0.12	0.02	0.03	0.07	0

*See Table 1 for the names of the health care regions.
†$p < 0.000$, ‡$p < 0.001$. (The p values are based on the χ^2 test after removing region 11; all p values are < 0.0000 when region 11 is included.)

chotropic drug combinations, 10% for prescriptions of benzodiazapines for more than 30 days and 6% for prescriptions of long-acting benzodiazepines. The highest prevalence of questionable psychotropic drug prescribing was in Québec–Chaudière and Saguenay–Lac Saint Jean; the lowest prevalence was in Montréal–Laval.

Discussion

We found that the three drug groups studied accounted for two thirds of all prescriptions and that 48% to 57% of the patients were given one or more drugs from each of these groups. Thus, prevalence of use likely explains why these three drug groups are commonly implicated in drug-related illness. Also, we found that 52.6% of the patients had at least one high-risk prescribing event in 1990 and that 45.6% experienced at least one episode of questionable high-risk prescribing. Both rational and questionable high-risk prescribing increased with patient age up to 75 to 84 years, primarily because of age-related increases in prescribing. These data are consistent with the hypothesis that the relation between drug-related illness and age is due to increases in the use of medications as patients become older as well as age-related increases in the prevalence of rational high-risk prescribing to achieve therapeutic efficacy. The reduction in the proportion of drug use among patients over 84 years may be a function of more conservative prescribing for patients in this age group or selective differences in the health status of patients who surpass average life expectancy, or both. Our findings also support Ferguson's[21] contention that questionable prescribing is common in the elderly population, and the increasing occurrence of drug-related illness with age may be explained in part by suboptimal prescribing practices.

In our study high-risk prescriptions, particularly of psychotropic drugs and NSAIDs, were more common among the women than among the men. These differences were a function of drug use: more women than men were prescribed drugs in these categories. A number of studies have found that women use more medication than men.[46–51] Consistent with this trend, drug-related illness has been noted to occur more commonly in women.[15,16,26,52] Reasons for differences in drug use between the sexes have been proposed by a number of authors, the most common explanation being that women visit physicians more often than men do.[50] In Quebec in 1990 a higher proportion of elderly women than of elderly men visited a physician; however, in the study sample the actual frequency of physician visits by the male and female patients was about equivalent.

Consistent with other studies, we found that questionable prescribing of psychotropic drugs was common,[22,53–55] particularly of benzodiazapines. We estimated that almost 33% of elderly people in Quebec in 1990 were exposed to benzodiazepines for more than 30 consecutive days and that 13% were prescribed long-acting benzodiazepines. The cut-off point of 30 days may be considered unnecessarily restrictive; however, more lenient cut-off points would not have substantially changed the prevalence. Among the patients who took benzodiazepines for more than 30 days, the average number of consecutive days of exposure was 141 days; this represents 4.5 prescriptions on average being filled during the longest consecutive period of use.

The prevalence of benzodiazepine use in our study was substantially higher than that reported in other population studies.[6,41,48] For example, in Saskatchewan in 1989 and in Britain in the early 1970s, 20% of elderly women and 10% to 12% of elderly men received a prescription for benzodiazapines.[6,41] The corresponding figures in our study were 51% and 33%. Even when these estimates are corrected for differences in sampling methods, the elderly patients in Quebec were more than twice as likely to be prescribed benzodiazepines in 1990 as elderly patients in Saskatchewan in the same period.[6] These findings were not explained by the preferential prescription of benzodiazepines over other categories of psychotropic drugs. The overall prevalence of psychotropic drug use in our study was 48.2%, whereas it was 10% to 33% in other studies.[56] Also, sedative-hypnotic drug use has been consistently highest in Quebec in three consecutive national health surveys.[46] The higher prevalence of psychotropic drug use among Quebec elderly patients does not seem to be explained by a higher prevalence of mental health problems. In 1988, 1.1% of Quebec elderly people were admitted because of a psychiatric problem, as compared with 1.7% in Saskatchewan and 1.3% in all of Canada.[57]

The fact that the patients in the remote region of Nord du Québec had the lowest prevalence of high-risk prescribing in all drug categories may have been because of reduced access to medical services and differences in the way medical services and drugs are reimbursed and thus recorded. In 1990 there was one physician per 1900 people in this region, as compared with 1 per 835 in Côte Nord and 1 per 267 in Montreal–Laval.[58] About 33% of medical services in this region are reimbursed on a salary basis, as compared with 3% to 15% in the other regions, and drugs may often be dispensed through nursing stations and health centres and therefore would not be recorded in the RAMQ prescription database.[37]

In summary, we found that high-risk prescribing was common in the elderly population and that questionable prescribing of psychotropic drugs was the most prevalent form of high-risk prescribing. We suspect that questionable high-risk prescribing may contribute to an increased risk of drug-related illness in elderly people and believe that this should be confirmed in future study. Potential reasons for the occurrence of questionable prescribing need to be explored so that interventions can be effectively implemented. By using administrative databases in our study we could not assess clinical indications for prescribing or patient compliance (actual expo-

sure to risk). The prevalence of questionable drug combinations representing therapeutic duplications (two or more drugs prescribed from the same class) may be overestimated, since medication substitutions cannot be differentiated from concurrent use. Despite these limitations, provincial prescription databases in Canada represent a unique resource for estimating medication use and cost in the elderly population and for estimating some of the determinants of use and the consequences.

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References

1. Sova G: *1989 Corpus Almanac and Canadian Sourcebook*, vol 1, Corpus Information Services, Don Mills, Ont, 1989
2. Williams P, Rush DR: Geriatric polypharmacy. *Hosp Pract* 1986; 21: 109–120
3. Jennett PA, Cooper M, Edworthy S et al: Consumer use of office health care: facts and implications. *Proceedings of the 5th ACMC Conference on Physician Manpower, Apr 28, 1991*, Association of Canadian Medical Colleges, Ottawa, 1991
4. Roos NP, Shapiro E: The Manitoba Longitudinal Study on Aging — preliminary findings on health care utilization by the elderly. *Med Care* 1981; 19: 644–657
5. Gordon M: Principles in prescribing for the older patient. *Drug Protoc* 1987; 2: 15–24
6. Quinn K, Baker MJ, Evans B: A population-wide profile of prescription drug use in Saskatchewan, 1989. *Can Med Assoc J* 1992; 146: 2177–2186
7. Nolan L, O'Malley K: Prescribing for the elderly. Part 1: Sensitivity of the elderly to adverse drug reactions. [review] *J Am Geriatr Soc* 1988; 36: 142–149
8. Mulroy R: Iatrogenic disease in general practice: its incidence and effects. *BMJ* 1973; 2: 407–410
9. Hutchinson TA, Flegal KM, Kramer MS et al: Frequency, severity and risk factors for adverse drug reactions in adult outpatients: a prospective study. *J Chronic Dis* 1986; 39: 533–542
10. Hurwitz N: Predisposing factors in adverse reactions to drugs. *BMJ* 1969; 1: 536–539
11. May FE, Stewart RB, Cluff LE: Drug interactions and multiple drug administration. *Clin Pharmacol Ther* 1977; 22: 322
12. Karch FE, Lasagna L: Adverse drug reactions: a critical review. *JAMA* 1975; 234: 1236–1241
13. Levy M, Lipshitz W, Eliakim M: Hospital admissions due to adverse drug reactions. *Am J Med Sci* 1979; 227: 49–56
14. Seidl LG, Thornton GF, Smith JW et al: Studies on the epidemiology of adverse drug reactions: III. Reactions in patients on a general medical service. *Bull Johns Hopkins Hosp* 1966; 19: 299–315
15. Grymonpre RE, Mitenko PA et al: Drug-associated hospital admissions in older medical patients. *J Am Geriatr Soc* 1988; 36: 1092–1098
16. Col N, Fanale JE, Kronholm P: The role of medication noncompliance and adverse drug reactions in hospitalizations of the elderly. *Arch Intern Med* 1990; 150: 841–845
17. Atkinson L, Gibson I, Andrews J: An investigation into the ability of elderly patients continuing to take prescribed drugs after discharge from hospital and recommendations concerning improving the situation. *Gerontology* 1978; 24: 225–234
18. Eustace CA, Johnson GJ, Gault MH: Improvements in drug prescription labels for patients with limited education or vision. *Can Med Assoc J* 1982; 127: 301–302
19. Gianetti V: Medication utilization problems among the elderly. *Health Soc Work* 1983; 8: 262–270
20. Zonderman AB, Leu VL, Costa PT: Effects of age, hypertension history and neuroticism on health perceptions. *Exp Gerontol* 1986; 21: 449–458
21. Ferguson JA: Patient age as a factor in drug prescribing practices. *Can J Aging* 1990; 9: 278–295
22. Shorr RI, Bauwens SF, Landefeld CS: Failure to limit quantities of benzodiazepine hypnotic drugs for outpatients: placing the elderly at risk. *Am J Med* 1990; 89: 725–732
23. Brook RH, Kamberg CJ, Mayer-Oakes A et al: *Appropriateness of Acute Medical Care for the Elderly*, Rand Corporation, Santa Monica, Calif, 1989: 1–58
24. Ives TJ, Bentz EJ, Gwyther RE: Drug-related admissions to a family medicine inpatient service. *Arch Intern Med* 1987; 147: 1117–1120
25. Colt HG, Shapiro AP: Drug-induced illness as a cause for admission to a community hospital. *J Am Geriatr Soc* 1989; 37: 323–326
26. Caranosos GJ, Stewart RB, Cuff LE: Drug-induced illness leading to hospitalization. *JAMA* 1974; 228: 713–717
27. Taggart HMcA: Do drugs affect the risk of hip fractures in elderly women? *J Am Geriatr Soc* 1988; 36: 1006–1010
28. Sloan RW: Alternative first line therapies in geriatric hypertension. *Geriatrics* 1989; 44 (4): 61–74
29. Larson EB, Kukull WA, Buchner D et al: Adverse drug reactions associated with global cognitive impairment in elderly persons. *Ann Intern Med* 1987; 107: 169–173
30. MacDonald JB, MacDonald ET: Nocturnal femoral fracture and continuing widespread use of barbituate hypnotics. *BMJ* 1977; 2: 483–485
31. Tinetti ME, Speechley M, Ginter SF: Risk factors for falls among elderly persons living in the community. *N Engl J Med* 1988; 319: 1701–1707
32. Ray WA, Griffin MR, Schaffner W et al: Psychotropic drug use and the risk of hip fracture. *N Engl J Med* 1987; 316: 363–369
33. Goodwin JS, Regan M: Cognitive dysfunction associated with naproxen and ibuprofen in the elderly. *Arthritis Rheum* 1982; 25: 1013–1015
34. Bigelow W, Collins T: Impact of nonsteroidal anti-inflammatory agents on general gastrointestinal upset in an elderly population. In Edlevitch SA (ed): *Pharmacoepidemiology*, vol 1, Lewis Pub, Chelsea, Mich, 1989: 243
35. Buechler JR, Malloy W: Drug therapy in the elderly: how to achieve optimum results. *Postgrad Med* 1989; 85: 87–99
36. Miller RR: Hospital admissions due to adverse drug reactions. *Arch Intern Med* 1974; 134: 219–223
37. *Statistiques annuelles 1990*, Service des communications, Régie de l'assurance-maladie du Québec, Quebec, 1990: 1–280
38. *Profil des divisions et subdivisions de recensement du Québec : Partie A*, Statistics Canada, Ottawa, 1993
39. Tatro DS (ed): *Drug Interaction Facts*, Facts & Comparisons Inc, St. Louis, 1992
40. Blazer D, George L, Hughes D: The epidemiology of anxiety disorders: an age comparison. In Salzman C, Leibowitz B (eds): *Anxiety Disorders in the Elderly*, Springer Publishing, New York, 1991: 17–30
41. Sheikh JI: Anxiety disorders and their treatment. *Clin Geriatr Med* 1992; 8: 411–426
42. Oswald I: Drugs and sleep. *Pharmacol Rev* 1968; 20: 273–303
43. Grantham P: Benzodiazepine abuse. *Br J Hosp Med* 1987; 37: 292–300
44. Busto U, Pharm D, Sellers EM et al: Withdrawal reaction after long-term therapeutic use of benzodiazepines. *N Engl J Med* 1992; 115: 854–859
45. Paulus HE: Clinical pharmacology of the anti-rheumatic drugs. In Schumacher HR Jr (ed): *Primer on the Rheumatic Disease*, 9th ed, Arthritis Foundation, Atlanta, 1988: 282–288
46. Rawson NSB, D'Arcy C: Sedative hypnotic drug use in Canada. *Health Rep* 1991; 3: 33–57

47. Beers MH, Ouslander JG, Fingold SF et al: Inappropriate medication prescribing in skilled-nursing facilities. *Ann Intern Med* 1992; 117: 684–689
48. Aoki FY, Large GW, Hildahl VK et al: Aging and heavy drug use: a prescription survey in Manitoba. *J Chronic Dis* 1983; 36: 75–84
49. Skegg DCG, Doll R, Perry J: Use of medicines in general practice. *BMJ* 1977; 1: 1561–1563
50. Hohmann AA: Gender bias in psychotropic drug prescribing in primary care. *Med Care* 1989; 27: 478–490
51. Kurfees JF, Dotson RL: Drug interactions in the elderly. *J Fam Pract* 1987; 25: 477–488
52. Griffin MR, Piper JM, Daugherty JR et al: Nonsteroidal anti-inflammatory drug use and increased risk for peptic ulcer disease in elderly persons. *Ann Intern Med* 1991; 114: 257–263
53. Gabe J: Towards a sociology of tranquillizer prescribing. *Br J Addict* 1990; 85: 41–48
54. Wilford BB: Abuse of prescription drugs. *West J Med* 1990; 152: 609–612
55. Maronde RF, Seibert S, Katzoff J et al: Prescription data processing — its role in the control of drug abuse. *Calif Med* 1972; 117: 22–28
56. Pérodeau GM, King S: Stress and psychotropic drug use among the elderly: an exploratory model. [review] *Can J Aging* 1992; 11: 347–369
57. Canadian Centre for Health Information: Mental health statistics. *Health Rep* 1990; 2 (suppl 3): 23–40
58. Savoie R: *Rapport annuel 1990–1991*, Corporation professionnelle des médecins du Québec, Quebec, 1991: 1–80

Appendix 1: High-risk drug combinations classified as rational or questionable for use in elderly patients*

Rational combinations

Cardiovascular
- ß-blocker + barbiturate
- ß-blocker + chlorpromazine
- ß-blocker + thioridazine
- ß-blocker + cimetidine
- ß-blocker + hydralazine
- ß-blocker + NSAID
- ß-blocker + propafenone
- ß-blocker + rifampin
- ß-blocker + prazosin
- ß-blocker + antithyroid drug
- Clonidine + tricyclic antidepressant
- Digitalis + furosemide
- Digitalis + ethacrynic acid
- Digitalis + thiazide
- Digitalis + antithyroid drug
- Digitalis + thyroid preparation
- Digitalis + cholestyramine
- Digitalis + quinidine
- Digitalis + amiodarone
- Digitalis + propafenone
- Amiodarone + warfarin
- Amiodarone + phenytoin
- Amiodarone + procainamide
- Quinidine + barbiturate
- Quinidine + cimetidine
- Quinidine + rifampin
- Verapamil + digitalis
- Cholestyramine + warfarin
- Clofibrate + warfarin
- Thyroxine + warfarin
- Thyroxine + digitalis
- Guanethidine + chlorpromazine
- Guanethidine + tricyclic antidepressant
- Thiazide + lithium
- Thiazide + sulfonemide oral hypoglycemic
- Indapamide + lithium
- Indapamide + digitalis
- Indapamide + sulfonemide oral hypoglycemic
- Thiazide + diazoxide
- Indapamide + diazoxide
- Diazoxide + lithium
- Mexiletine + theophylline
- Digoxin + erythromycin
- Digoxin + metoclopramide
- Digoxin + quinine

Psychotropic
- Clonazepam + antidepressant
- Other benzodiazepine + antidepressant
- Clonazepam + tranquillizer†
- Other benzodiazepine + tranquillizer
- Clonazepam + opiate
- Other benzodiazepine + opiate
- Clonazepam + barbiturate
- Other benzodiazepine + barbiturate
- Clonazepam + sedative‡
- Sedative + tranquillizer
- Sedative + opiate
- Sedative + antidepressant
- Tranquillizer + cardiotropic drug
- Tranquillizer + opiate
- Tranquillizer + antidepressant
- Tranquillizer + barbiturate
- Tranquillizer + propranolol
- Tranquillizer + opiate
- Barbiturate + warfarin
- Barbiturate + quinidine
- Barbiturate + valproic acid
- Barbiturate + ß-blocker
- Tricyclic antidepressant + barbiturate
- Tricyclic antidepressant + tranquillizer
- Tricyclic antidepressant + clonidine
- Tricyclic antidepressant + guanethidine
- Tricyclic antidepressant + opiate
- Tricyclic antidepressant + clonazepam
- Tricyclic antidepressant + other benzodiazepine
- Tricyclic antidepressant + sedative
- MAO inhibitor + clonazepam
- MAO inhibitor + other benzodiazepine
- MAO inhibitor + barbiturate
- MAO inhibitor + tranquillizer
- Tricyclic antidepressant + cimetidine

NSAID
- ASA + valproic acid
- ASA + probenecid
- ASA + sulfinpyrazone
- ASA + heparin
- ASA + oral hypoglycemic
- ASA + antidiabetic agent
- ASA + methotrexate
- NSAID + ACE inhibitor
- ASA + hydrocortisone
- NSAID + ß-blocker
- ASA + corticosteroid

Questionable combinations

Cardiovascular
- Two ß-blockers
- Two calcium-channel blockers
- Two ACE inhibitors
- Thiazide + thiazide
- ß-blocker + theophylline
- ß-blocker + verapamil
- Ethacrynic acid + furosemide
- Furosemide + furosemide
- Two potassium-sparing diuretics
- Potassium-sparing diuretic + potassium supplement
- Indapamide + thiazide

Psychotropic
- Clonazepam + other benzodiazepine
- Other benzodiazepine + benzodiazepine
- Clonazepam + clonazepam
- Benzodiazepine + sedative
- Sedative + barbiturate
- Two sedatives
- Two tranquillizers
- Two barbiturates
- Barbiturate + opiate
- Barbiturate + antidepressant
- MAO inhibitor + levodopa
- MAO inhibitor + meperidine
- MAO inhibitor + antidepressant
- Two MAO inhibitors
- Two tricyclic antidepressants

NSAID
- ASA + warfarin
- Two NSAIDs
- ASA + ASA

*See Table 2 for a definition of rational and questionable high-risk prescribing. MAO = monoamine oxidase, ACE = angiotensin-converting enzyme.