

The Development of a Prescription Drug Dependence Screen for Older Adults

Ruby E. Grymonpre, Mark Badger, Ellen Tabisz, W.R. Jacyk and Colin Powell

ABSTRACT

The Manitoba Drug Dependence Screen (MDDS) was developed as a standardized instrument to identify elderly persons at risk of prescription drug dependence. As a preliminary test, the Manitoba Drug Dependence Screen was administered to persons aged 65 years or older presenting to the Emergency Room of an 860-bed teaching hospital. Sixty-one (15%) of the 407 subjects screened positive for possible prescription drug dependence with 38 patients (9%) deemed to be possibly dependent on benzodiazepines and 23 patients (6%) possibly dependent on opiates. The number of prescription drugs reported was the only demographic or behavioural variable which had a statistically significant relationship with dependence. Although a larger percentage of women reported benzodiazepine and opiate use, an equal proportion of men and women users had possible dependence to these drugs.

The results of this preliminary test suggest that the Manitoba Drug Dependence Screen is not without inaccuracies and that further validation and modification is necessary. Once the screening instrument has been appropriately refined, the MDDS may find use in both clinical and research settings.

Keywords: Prescription Drug Dependence, Benzodiazepines, Opioids, Screening instrument, Elderly

RÉSUMÉ

Le test de dépistage de pharmacodépendance du Manitoba a été créé comme outil standardisé pour identifier les personnes âgées qui présentaient un risque d'accoutumance aux produits d'ordonnance. Il a été administré comme test préliminaire à des personnes de 65 ans ou plus qui se présentaient à l'urgence d'un hôpital de 860 lits. Des 407 personnes âgées soumises au test, 61 (15 %) ont eu des résultats positifs. De ce nombre, 38 (9%) ont été évaluées comme présentant une dépendance probable aux benzodiazépines et 23 autres (6%) comme une dépendance probable aux opiacés. Le nombre de médicaments d'ordonnance rapporté était la seule variable démographique ou comportementale qui avait un lien statistiquement significatif avec la pharmacodépendance. Bien qu'un plus fort pourcentage de femmes ait indiqué faire usage de benzodiazépines et d'opiacés, un pourcentage égal d'hommes et de femmes présentaient une dépendance probable à ces médicaments.

Les résultats de ce test préliminaire portent à croire que le test de dépistage de pharmacodépendance du Manitoba n'est pas

sans faille, qu'il doit faire l'objet d'une validation plus rigoureuse et que des ajustements sont nécessaires. Une fois que cet outil de dépistage aura été correctement mis au point, il pourrait trouver des applications utiles en recherche et en clinique.

Mots clés: dépendance aux médicaments d'ordonnance, benzodiazépines, opiacés, test de dépistage, personnes âgées.

Can J Hosp Pharm 1996;49:7-12

INTRODUCTION

Aging is often accompanied by several crises such as loss of loved ones, loneliness, poor health, and intellectual decline. As a result, mental health disorders such as insomnia, anxiety, and depression are common in the elderly and psychoactive drugs are often prescribed.¹ A potential consequence of chronic benzodiazepine (BZ) or opiate (OP) drug therapy is physiologic dependence defined as the development of signs and symptoms of a withdrawal reaction upon the abrupt discontinuation of the drug. The DSM III-R clearly differentiates physiologic dependence from "Psychoactive Substance Dependence" where a person has "impaired control of psychoactive substance use and continues use of the substance despite adverse consequences."² Indeed,

Ruby E. Grymonpre, PharmD, is Associate Professor in the Faculty of Pharmacy, University of Manitoba, Winnipeg, Manitoba.

Mark Badger, MA, is in the Department of Social Work at St. Boniface General Hospital, Winnipeg, Manitoba.

Ellen Tabisz, MSW, is in the Department of Social Work at St. Boniface General Hospital, Winnipeg, Manitoba.

W.R. Jacyk, MD, FRCP, is in the Department of Medicine at St. Boniface General Hospital, Winnipeg, Manitoba.

Colin Powell, MB, FRCP (Edin), FRCP (Glas), is in the Department of Medicine at St. Boniface General Hospital, Winnipeg, Manitoba.

Address Correspondence to: Dr Ruby Grymonpre, Faculty of Pharmacy, University of Manitoba, Winnipeg, Manitoba R3T 2N2

Acknowledgements: The authors would like to thank Elizabeth Payne, Lois Lindblom and Deb Kostyk for their help in this study. This study was partly funded by a grant provided by Sandoz Canada, Inc. and a Research Fellowship from the Centre of Aging, University of Manitoba.

many persons with physiologic dependence will not have a psychoactive substance use disorder.²

Studies which evaluate psychotropic prescribing patterns confirm that a large percentage of the elderly are chronic consumers of BZs and OPs.^{1,3,4} However, the prevalence of physiologic dependence in the elderly to these psychotropic agents also described as prescription drug dependence (PDD) is unknown. Such drug utilization studies likely overestimate the extent of PDD in the elderly since not all persons prescribed psychotropic drugs develop physiologic dependence.²

The initial step in the treatment and/or prevention of unnecessary PDD is the identification of those at risk. It is likely that many individuals are not being treated for drug dependence problems merely because this aspect of chronic BZ or OP use is unrecognized.

The Elders Health Program was a three-year demonstration project involved in the identification, intervention, and treatment strategies for substance use management in the elderly. Shortly after initiating this project it became apparent that PDD to BZs and OPs was not being detected in a systematic and standardized way. Although a number of screening instruments demonstrating reasonable validity were available as a means of identifying patients with psychoactive substance dependence to alcohol⁵⁻⁷ including the Michigan Alcohol Screening Test (MAST) which had recently been validated for use in the elderly⁸ this did not deal with PDD. Furthermore, the Drug Abuse Screening Test (DAST), which is an instrument to screen for psychoactive substance dependence to drugs with emphasis on the social, occupational, psychological, or physical problems secondary to drug abuse,⁹ was deemed, by our group, to be inappropriate for older individuals where physiologic dependence may be the predominant concern and the behaviours commonly associated with the DSM III-R substance use disorder do not apply. Hence, none of the existing instruments were appropriate to identify elderly persons at risk of PDD.

The objective of this project was to design and conduct a preliminary test of a screening instrument for use in the elderly to identify persons at risk of physiologic dependence to BZs and OPs.

METHODS

Development of the Manitoba Drug Dependency Screen

The Manitoba Drug Dependency Screen (MDDS) was constructed by the authors and evaluated by 12 Canadian physicians and pharmacists with expertise or interest in the area of chemical dependency. Their recommendations were used to modify the questionnaire which was then administered in a pilot test for one month.

The pilot test identified the need for several revisions relevant to wording and format of the instrument. These revisions were made prior to the use of the screen in the preliminary test. It also became apparent from the pilot that several subjects did not know the name or dose of their medications. To minimize the problem, a colour photograph section of all BZs and OPs illustrated in the Compendium of Pharmaceuticals and Specialties¹⁰ was appended to the MDDS (with written permission from the Canadian Pharmaceutical Association).

The basis of the MDDS is the calculation of a Cumulative Benzodiazepine Exposure (CBE) for persons reporting BZ use or the Cumulative Opiate Exposure (COE) for persons reporting use of an OP (Table I). These equations have been adapted from Harrison et al.¹¹ who developed the CBE for detoxification of high-dose BZ abusers. The calculations incorporate an equivalence factor for BZs other than diazepam or for OPs other than morphine. The determination of equipotent doses within and between drug categories was difficult to establish due to the wide interpatient variability in response to the BZs and OPs, especially in the aging population. For the purposes of the MDDS, diazepam equivalencies were based on the recommended anxiolytic dose of each BZ, consistent with Harrison et al.¹¹ A comparable dose of triazolam in anxiety was difficult to determine due to its short half-life, and we chose an equivalence factor of 10 for triazolam. Commonly cited equivalent doses of the OPs compared with morphine are also used for this preliminary ques-

Table I: Calculations for the Cumulative Benzodiazepine and Cumulative Opiate Exposures

<p>CBE^a = DRUG DOSE^b x DIAZEPAM EQUIVALENCE^c x DURATION^d</p> <p>PHYSIOLOGIC DEPENDENCE IS:</p> <p>UNLIKELY IF CBE THE IS < 1,000 mg</p> <p>POSSIBLE IF THE CBE IS ≥ 1,000 mg</p> <p>^a CBE is the Cumulative Benzodiazepine Exposure in mg</p> <p>^b DRUG DOSE is the oral dose in mg/day</p> <p>^c if drug is not diazepam, incorporate DIAZEPAM EQUIVALENCE FACTOR</p> <p>^d DURATION is the number of DAYS of REGULAR DAILY use. If use is not DAILY, then categorize as IRREGULAR USE</p>
<p>COE^a = DRUG DOSE^b x MORPHINE EQUIVALENCE^c x DURATION^d</p> <p>PHYSIOLOGIC DEPENDENCE IS:</p> <p>UNLIKELY IF COE THE IS < 500 mg</p> <p>POSSIBLE IF THE COE IS ≥ 500 mg</p> <p>^a COE is the Cumulative Opioid Exposure in mg</p> <p>^b DRUG DOSE is the oral dose in mg/day</p> <p>^c if drug is not morphine, incorporate MORPHINE EQUIVALENCE FACTOR</p> <p>^d DURATION is the number of DAYS of REGULAR DAILY use. If use is not DAILY, then categorize as IRREGULAR USE</p>

tionnaire.¹² The equivalence factors for the various BZs and OPs are shown in Table II.

The use of the CBE or COE as the determinant of physiologic dependence assumed the following:

- the likelihood of developing a withdrawal reaction to the BZs and OPs depends on the dose, duration, and regularity of use of these agents.¹
- all BZs are likely to cause physiologic dependence although the withdrawal reaction may be more severe in patients using BZs with a short half-life.¹
- opiate dependency appear to be mediated via a different receptor site as compared with the benzodiazepines.¹ Therefore, the COE is not additive with the CBE.

The minimum CBE value for possible PPD to BZ was 1,000 mg. This value was based on the determination of the CBE in 25 case reports of BZ withdrawal reactions.¹³ In all of these case reports, the CBE was greater than 1,000 mg and most commonly greater than 5,000 mg. The minimum COE value for possible PDD to OPs was 500 mg, based on literature suggesting that greater than 50% of patients develop physiologic dependence after 10 days of therapy with morphine sulphate 10 mg intramuscularly every four hours¹⁴ as well as the statement that “repeated doses of 60 mg or more of morphine sulphate per day for 30 or more days are associated with the development of physiologic dependence.”¹²

The data necessary to calculate a CBE or COE included the drug name, the dose reported to be taken by patient,

frequency of use throughout the day or week, and duration of use. These data were obtained through a questionnaire designed to solicit information pertinent to prescription and nonprescription medications currently being taken with particular emphasis on medications for “sleep”, “nerves”, or “pain”. As well, information on certain behaviours or ideas was incorporated into the MDDS.

Preliminary Test of the MDDS

Persons 65 years of age and older presenting to the St. Boniface General Hospital emergency room between 0800 and 1600 hours were screened for chemical dependency problems. The screening process used for the project is described in a paper previously published.¹⁵ Briefly, a social worker was responsible for the administration of the two alcohol screening tools, the BMAST (Brief Michigan Alcoholism Screening Test) and the CAGE and the administration of the MDDS to test for physiologic dependence to BZs or OPs. The social worker received a brief orientation on the use of the MDDS prior to the pilot project. Completed questionnaires were given to the clinical pharmacist for scoring.

Funding to perform urine drug screens became available in May 1989. Thereafter, whenever subjects were willing and able, a urine drug screen to determine the presence of OPs and BZs in the urine was obtained in the same persons. Urine specimens were analyzed using E.M.I.T. kits (Syva Co., Palo Alto, CA) employed on a Hitachi 717 Clinical Analyzer (Boehringer Mannheim, Canada, Dorval, Quebec). Drug screens were considered negative at levels below 300 ng/mL.

Analysis of gender by reporting use of at least one prescription medication, one BZ or one OP was done. The proportion of subjects with possible PDD to BZs or OPs, as determined by the MDDS, was calculated. Associations between the percentage of persons with possible PDD and age, sex, and number of prescribed drugs were determined in an effort to identify factors predisposing to the risk of drug dependence. Behaviours thought to coexist with drug dependence including current alcohol abuse (as determined from the BMAST and CAGE questionnaires), doctor or pharmacy shopping, an indication by the patient that medications were not working as well as they used to, or patient desire to do without the medications were also compared between subjects categorized as possible PDD, unlikely PDD, and those persons who reported no use of BZ or OP (negative PDD). Statistical analyses were performed using the Statistical Package for the Social Sciences.¹⁶ Chi-square and t-tests were employed to examine the relationships between variables. Statistical significance was defined as $p < 0.05$. The results of the urine drug screen were used for comparison to the findings of the drug dependency screen.

Table II: Diazepam and Morphine Equivalence Factors

Benzodiazepine	Diazepam Equivalence Factor
Alprazolam	20
Bromazepam	1.7
Chlordiazepoxide	0.2
Clonazepam	2.5
Clorazepate	1.3
Diazepam	1.0
Flurazepam	0.3
Lorazepam	5
Nitrazepam	2
Oxazepam	0.2
Temazepam	0.7
Triazolam	10
Opiate	Morphine Equivalence Factor
Codeine	.03
Hydromorphone	8
Levorphanol	19
Meperidine	0.2
Morphine	1.0
Oxycodone	2
Oxymorphone	10
Pentazocine	0.2
Propoxyphene	0.5

Written, informed consent was obtained prior to all interviews. The protocol was reviewed and approved by the University of Manitoba, Faculty Committee on the Use of Human Subjects in Research.

RESULTS

During the study period, October 1988 to November 1989, 641 subjects were available for interview. This represented approximately 50% of all patients, 65 years of age or older, who presented to the emergency room between these months. A large proportion of patients eligible by age could not participate due to language barriers, cognitive impairment, severe illness, or presentation to emergency between 1600 and 0800 hours. Of the 641 subjects available for study, 491 (77%) were willing to provide written informed consent. During the month of October 1988, 84 subjects participated in the pilot project and following alterations to the form, 407 additional subjects were recruited. This paper presents data on those 407 subjects. Urine samples were collected for drug analyses on 124 of the 407 subjects.

Demographic data are presented in Table III. There was no difference in the mean age between men and women. However, women reported using a greater number of prescribed drugs (3.2 vs 2.7; $p < 0.01$). Although an equal proportion of men and women reported taking at least one prescribed drug, a larger proportion of women reported using at least one BZ (29% vs 15% $p < 0.001$) compared to men, and women were also more likely to report use of at least one OP (18% vs 9% $p < 0.05$).

Sixty-one (15%) of the 407 subjects had possible PDD, 38 (9%) patients with a possible dependence to BZ and 23 (6%) patients with a possible dependence to OP. Of the BZ users, an equal percentage of women and men were considered dependent (41% vs 43%, respectively). Simi-

larly, women OP users were equally as likely as men users to be dependent on these drugs (38% vs 47%).

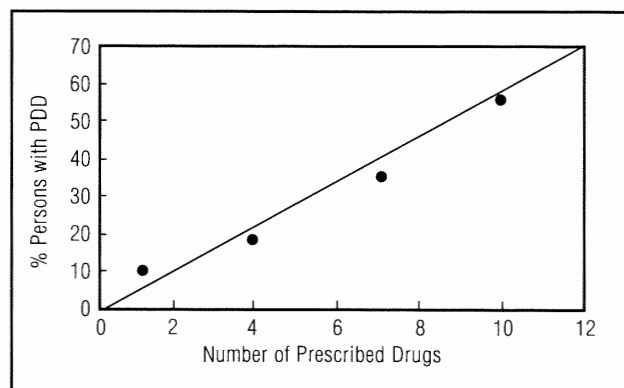
Behaviours thought to coexist with drug dependence were compared among three groups: (1) those persons not taking a BZ or OP (negative PDD), (2) persons with a possible PDD problem, and (3) those persons with an unlikely PDD problem or irregular use of BZ/OP. The only significant relationship identified was that persons with unlikely PDD or irregular use were more likely to indicate that their medicines were not working as well as they used to (15% vs 13% vs 28% for negative, positive and unlikely/irregular use PDD respectively $p < 0.05$). Other patient behaviours such as indicating a desire to do without medications, receiving medicines from more than one physician or pharmacist, and current alcohol abuse were not more common for any group. There was no association between the mean number of drugs reported by age. The percentage of persons with possible PDD also did not correlate with age. However, there was a strong correlation between the percentage of persons with PDD and the number of drugs reported ($p < 0.0001$; Chi-square = 72.06) (Figure 1).

The results of the 124 urine drug screens are presented in Table IV. Of the 89 subjects who reported not using BZs or OPs (negative PDD), 12 (13%) had urine which was positive for these substances. Of the 15 persons with possible PDD, five (33%) had a negative urine for the substance in question. Urine drug screen results were available for 20 persons with unlikely/irregular PDD and the urine drug screen results from these subjects are mixed.

Table III: Demographic Data on Study Patients

	MALES N = 185	FEMALES N = 222	P VALUE
AGE (years)			
MEAN	74.6 ± 6.6	75.2 ± 6.5	NS
RANGE	65 - 92	65 - 95	
NUMBER OF DRUGS REPORTED			
MEAN	2.7 ± 2.0	3.2 ± 2.3	<0.01
RANGE	0 - 10	0 - 14	
N (%) REPORTING			
AT LEAST ONE DRUG	156 (84)	198 (89)	NS
N (%) REPORTING			
AT LEAST ONE BZ	28 (15)	64 (29)	<0.001
N (%) REPORTING			
AT LEAST ONE OP	17 (9)	39 (18)	<0.05

Figure 1: Percent of Persons with PDD versus number of prescription drugs reported



PDD = prescription drug dependence

Table IV: Results of Urine Drug Screen

	POSSIBLE PDD N = 15	NEGATIVE PDD N = 89	UNLIKELY PDD N = 20
positive urine	10 (67%)	12 (13%)	11 (55%)
negative urine	5 (33%)	77 (87%)	9 (45%)

DISCUSSION

This report describes the development and preliminary testing of a standardized instrument, the MDDS, to screen for physiologic dependence to BZs and OPs in the elderly. For this developmental phase, no attempt was made to compare the findings of the MDDS to a more rigorous assessment of prescription drug dependence and further validation is necessary.

The instrument is intended to identify risk of physiologic dependence. It is not designed to determine the appropriateness of the chronic BZ or OP therapy prescribed. In general, BZs and OPs are safe and effective, and patients with severe, disabling, chronic anxiety or pain may have a "therapeutic" dependence to these agents. In situations of "therapeutic" dependence, the benefits of prolonged and continuous therapy outweigh the risks associated with physiologic dependence.^{17,18} Such individuals would likely be identified with possible PDD by the MDDS, however, upon further assessment, the clinician may decide to continue with the therapy prescribed. Some studies suggest that, especially in the older population, chronic psychotropic drug use is inappropriate.^{1,19-21} Patients may be using BZs chronically in the absence of an appropriate psychiatric or medical indication.^{19,20} Of 64 patients prescribed BZs in one study,¹⁹ 42 did not have a psychiatric condition and only one had an anxiety-related diagnosis. Elderly may be using psychotropic drugs to cope with aging issues.¹ Dependence may even be the reason for chronic psychotropic drug use where persons consume a drug to prevent experiencing symptoms of withdrawal.²⁰ Chronic insomnia is a major reason for long-term use of BZs, yet tolerance develops to the hypnotic efficacy of these agents and they also cause a substantial deterioration in the quality of sleep.²¹ These examples of inappropriate chronic psychotropic drug therapy may lead to a "morbid" physiologic dependence where the risks of chronic therapy likely outweigh any benefits. In such cases, the MDDS would facilitate referral for further assessment and treatment.

The screen was administered to 407 elderly subjects in this study. Nine percent of the study sample were considered to have possible PDD to a BZ and six percent of the sample screened were considered to have possible PDD to OPs. It is important to note that no subjects were identified with definite PDD since true physiologic dependence, as evidenced by signs and symptoms of a withdrawal reaction, was not specifically assessed. Whether subjects identified in this study had "therapeutic" or "morbid" physiologic dependence was also not determined. These findings are comparable to a survey of 379 non-institutionalized elderly living in Scotland.²⁰ Of those surveyed, 12% were regular users of sedative/hypnotics; 83% of these regular users felt they could not

do without their sleeping tablet although 70% were willing to try an alternative. Nearly half of these patients had tried stopping their tablets, but without success. In a separate study evaluating patients aged 65 years or older admitted to the psychiatric division of a New York Hospital, PDD was identified in 26% of patients.²² This higher percentage of dependence in this study compared to ours was likely due to differences in patient selection.

In some cases, it was felt that the MDDS underestimated the probability of PDD. One subject reported taking triazolam 0.125 mg daily for two years. The calculated CBE was 913 mg and PDD was deemed unlikely in this case. A second example was a subject who reported taking chlordiazepoxide 5 mg daily for two and a half years. Her CBE was also 913 mg and, again by our definition PDD was unlikely. The Diazepam/Morphine Equivalence Factors and the minimum CBE/COE for possible PDD (currently 1000 mg and 500 mg for BZs and OPs, respectively) will require further evaluation and modification.

In addition to estimating the extent of PDD in the elderly, the MDDS allowed for the identification of factors which may correlate with PDD. The number of prescription drugs reported was the only variable which had a statistically significant relationship with PDD. This supports the association between BZs and physical ill health previously reported.^{19,23} No correlation was seen between PDD and age. Neither was PDD associated with patient behaviours thought to coexist with drug dependence including doctor/pharmacy shopping, patient indication that medications were not working as well as they used to, or a patient's desire to do without medications. It is possible that some of these behaviours or ideas do not, in fact, correlate with PDD in older individuals. Although physiologic dependence commonly occurs with the DSM III-R disorder Psychoactive Substance Dependence, other behaviours such as a preoccupation with obtaining the substance (doctor or pharmacy shopping, for example) are necessary for the latter diagnosis.² Current alcohol abuse (as determined by the BMAST and CAGE) was also not predictive of PDD in this study. This finding is not consistent with a study by Busto et al²⁴ which suggested that BZs were more commonly "used and abused by alcoholics". Since the Busto study examined alcoholics of all ages, 75% of whom were male, the different demographic profile between the two study samples may provide an explanation for these conflicting findings.

The true accuracy (sensitivity, specificity, positive predictive value) of the MDDS could not be calculated in this study since the prevalence of true physiologic dependence in our population was unknown. Although a negative urine drug screen could essentially rule out physiologic dependence, a positive urine was not neces-

sarily diagnostic for dependence, thus prevalence rates could not be obtained from the urine drug screen. However, urine results did provide a general measure of the reliability of the MDDS.

The results of the urine drug screen suggested that false negative and false positive results can be expected with use of the MDDS. While the reason for these results is not clear it is probable that either intentionally or unintentionally patients will provide inaccurate information. Thirteen percent of 89 subjects who reported not taking BZs or OPs had a positive urine drug screen. Such potentially false negative results are undesirable for a screening instrument since these subjects would not be referred for further assessment. Thirty-three percent of the 15 subjects who were deemed to have possible PDD according to the MDDS had a negative urine drug screen. For a screening instrument, such false positive results are less of a concern since further assessment would rule out the clinical problem.

In this study, 87% of our elderly sample reported using at least one prescription drug with a mean of three drugs per person; 22% of our sample reported using at least one BZ. These data are consistent with most reports on drug use in community dwelling elderly.^{3,5} This study also confirms the findings of several other reports which indicate that psychotropic drug use is more prevalent in females.²⁶

In summary, the extent of PDD to BZ and OP in the community dwelling elderly was estimated using the newly developed MDDS. Factors predisposing to the risk of PDD were also identified. Before being used as a clinical or research tool, validation of the MDDS is required. It is hoped that use of this standardized screening instrument will facilitate early identification of physiologic dependence to BZs and OPs leading to further assessment of and, where appropriate, the management of inappropriate chronic BZ and OP use. Widespread use of the MDDS will also increase awareness of the problem and prevent the inappropriate use of these psychotropic agents. ☒

REFERENCES

1. Woods JH, Katz JL, Winger G. Abuse liability of the benzodiazepines. *Pharmacol Rev* 1987; 39:285-90.
2. Diagnostic and Statistical Manual of Mental Disorders 3rd ed-revised. American Psychiatric Association. Washington, D.C., 1987.
3. Prien RL. Problems and practices in geriatric psychopharmacology. *Psychosomatics* 1980; 21:213-23.
4. Grymonpre RE, Sitar DS, Montgomery PR, et al. Prescribing patterns for older heavy drug users living in the community. *DICP Ann Pharmacotheor* 1991; 25:186-90.
5. Selzer ML. The Michigan alcoholism screening test: The quest for a new diagnostic instrument. *Am J Psychiat* 1971; 127:1653-8.
6. Zung BJ. Factor structure of the Michigan alcoholism screening test. *J Stud Alcohol* 1978; 39:56-67.
7. Ewing JA. Detecting alcoholism: The CAGE questionnaire. *JAMA* 1984; 252:1905-7.
8. Willenbring ML, Christensen KJ, Spring WD, et al. Alcoholism screening in the elderly. *J Am Geriatr Soc* 1987; 35:864-9.
9. Skinner HA. The drug abuse screening test. *Addict Behav* 1982; 7:363-71.
10. Anon. Compendium of Pharmaceuticals and Specialties, 1988, Canadian Pharmaceutical Association.
11. Harrison M, Busto U, Naranjo CA, et al. Diazepam tapering in detoxification for high dose benzodiazepine abuse. *Clin Pharmacol Ther* 1984; 36:527-33.
12. Halpern LM. Analgesic drugs in the management of pain. *Arch Surg* 1977; 112:861-9.
13. Perry PJ. Assessment of addiction liability of benzodiazepines and buspirone. *Drug Intell Clin Pharm* 1985; 19:657-9.
14. Adams J. Adequate relief needed for patients with chronic cancer pain. *Drug Utiliz Rev* 1988; 4:57-62.
15. Jacyk WR, Tabisz E, Badger M, et al. Chemical dependency in the elderly: Identification phase. *Can J Aging* 1991; 10:10-7.
16. Norus MA SPSS/PC & V2.0 Base Manual, 1988, Michigan: SPSS Inc.
17. Taylor FK. The damnation of benzodiazepines. *Br J Psychiat* 1989; 154:697-704.
18. Nagy A. Long-term treatment with benzodiazepines: Theoretical, ideological and practical aspects. *Acta Psychiatr Scand* 1987; 76(suppl 335):47-55.
19. Rodrigo EK, King MB, Williams P. Health of long term benzodiazepine users. *Br Med J* 1988; 296:603-6.
20. Hay D, Milne RM, Gilleard CJ. Hypnotic drugs, old people and their habits: A general practice study. *Health Bull* 1986; 44:218-22.
21. Schneider-Helmert D. Why low-dose benzodiazepine-dependent insomniacs can't escape their sleeping pills. *Acta Psychiatr Scand* 1988; 78:706-11.
22. Whitcup SM, Miller F. Unrecognized drug dependence in psychiatrically hospitalized elderly patients. *J Am Geriatr Soc* 1987; 35:297-301.
23. Mellinger GD, Balter MB, Uhlenhuth EH. Prevalence and correlates of long-term regular use of anxiolytics. *JAMA* 1984; 251:375-9.
24. Busto U, Sellers EM, Sisson B, et al. Benzodiazepine use and abuse in alcoholics. *Clin Pharmacol Ther* 1982; 31:207-8.
25. Helling DR, Lemke JH, Semla TP, et al. Medication use characteristics in the elderly: The Iowa 65+ rural health study. *J Am Geriatr Soc* 1987; 35:4-12.
26. Cooperstock R. A review of women's psychotropic drug use. In: Howell E, Bayers M, eds. *Women and Mental Health*. New York: Basic Books Inc., 1981, 131-140.