ORIGINAL SCIENTIFIC PAPER

QUANTITATIVE RESEARCH

Potentially inappropriate medication use: the Beers' Criteria used among older adults with depressive symptoms

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ABSTRACT

INTRODUCTION: The ageing population means prescribing for chronic illnesses in older people is expected to rise. Comorbidities and compromised organ function may complicate prescribing and increase medication-related risks. Comorbid depression in older people is highly prevalent and complicates medication prescribing decisions.

AIM: To determine the prevalence of potentially inappropriate medication use in a community-dwelling population of older adults with depressive symptoms.

METHODS: The medications of 191 community-dwelling older people selected because of depressive symptoms for a randomised trial were reviewed and assessed using the modified version of the Beers' Criteria. The association between inappropriate medication use and various population characteristics was assessed using Chi-square statistics and logistic regression analyses.

RESULTS: The mean age was 81 (±4.3) years and 59% were women. The median number of medications used was 6 (range 1–21 medications). The most commonly prescribed potentially inappropriate medications were amitriptyline, dextropropoxyphene, quinine and benzodiazepines. Almost half (49%) of the participants were prescribed at least one potentially inappropriate medication; 29% were considered to suffer significant depressive symptoms (Geriatric Depression Scale ≥5) and no differences were found in the number of inappropriate medications used between those with and without significant depressive symptoms (Chi-square 0.005 p=0.54).

DISCUSSION: Potentially inappropriate medication use, as per the modified Beers' Criteria, is very common among community-dwelling older people with depressive symptoms. However, the utility of the Beers' Criteria is lessened by lack of clinical correlation. Ongoing research to examine outcomes related to apparent inappropriate medication use is needed.

KEYWORDS: Depression; depressive symptoms; inappropriate prescribing; older adults

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Introduction

It has been estimated that by 2030 the world population is likely to include 1 billion people over the age of 65 years, accounting for approximately 13% of the total world population.[1] Due to the higher prevalence of diseases in older people, they are more likely than their younger counterparts to be prescribed medications. Some studies have shown that, on average, medication use increases by 52% after the age of 65 years.[2] Several studies have shown an increased risk for medication-related morbidity and mortality, with a higher number of medications prescribed.[3–5]

Late-life depression is also common in older people, affecting between 17 and 30% of older community dwellers over the age of 65 years.[6] As

symptoms of depression in this population may be confounded by symptoms of comorbid chronic illnesses, or perceived as a natural progression of ageing, depression often goes undiagnosed.[6] Consequently, treatment of depression in this population, already complicated by ageing factors and medication-related issues, can be part of complex prescribing decisions.

Furthermore, a number of studies have suggested that medications are not always used appropriately in older people.[7–12] Individuals aged 65 years and older are more prone to adverse drug reactions than younger people.[13] Inappropriate use of medication in older adults may include the overuse of drugs, prescribing medications that are predicted to be poorly tolerated by the elderly, prescribing medications that are highly likely to exacerbate a clinical condition (e.g. recurrent falls from over-sedation with benzodiazepines) and underutilisation of appropriate medications (e.g. low-dose aspirin).[14,15] Those with depression are particularly at risk of adverse drug events, due to increased medications needed and increased comorbidity.[16]

Both explicit (e.g. Beers' Criteria[10]) and implicit (e.g. Medication Appropriateness Index[14]) instruments can be used to assess appropriate use of medications for older individuals in hospital and community settings. The biggest difference in application between the two instruments is that clinical expertise is required when using implicit criteria. The Medication Appropriateness Index, for example, measures prescribing appropriateness according to 10 short questions covering the indication, effectiveness, dose, administration, drug–drug interactions and drug–disease interactions and cost. The Beers' Criteria, on the other hand, defines inappropriate medications as those which should be avoided in older people, as the risks associated with their use outweigh their benefits.[10,12] The Beers' Criteria is divided into two lists which examine appropriateness of medication use in specific clinical conditions (condition-dependent list), and medications that are inappropriate regardless of the presence of a particular comorbidity (condition-independent list).[4,14,17–20] The lists identify specific drugs or drug prescriptions (excessive dose, excessive treatment duration, inappropriate drug combination and coexisting illness) with unfavourable benefit/risk ratio or questionable efficacy.[10,21–22] While the Beers' Criteria have been used worldwide to evaluate inappropriate medication prescribing, there are no currently available reports on its clinical utility or validity to assist with improving prescribing in elderly individuals with depression. In addition, geographic variation has been described,[23] with no comparable data in New Zealand (NZ).

WHAT GAP THIS FILLS

What we already know: Older people use many medications and the use of inappropriate medication is higher in those with mental health needs.

What this study adds: The study found that almost half of those recruited in a community sample of people with depressive symptoms were using inappropriate medications according to the Beers' Criteria. Outcomes related to medication use are needed to fully understand the risk from inappropriate use as identified by use of the Beers' Criteria.

In this paper, we report a community-based study assessing the potentially inappropriate use of medications according to the Beers' Criteria among community-dwelling elderly subjects with symptoms of depression. The aims of this study are:

a. to describe the pattern of medication use in older people with depressive symptoms at enrolment;
b. to assess medication inappropriateness in all enrolled participants using a modified version of the Beers' Criteria to reflect the NZ context; and
c. to contrast the use of inappropriate medication in older individuals with and without significant depressive symptoms.

Methods

Data sources and study population

The medications used by 193 elderly people enrolled in the Depression in Late Life Intervention Trial of Exercise (DeLLITE) study[24,25] were used as our data source. The DeLLITE study enrolled people aged 75 years and over living in the community who agreed to participate in a trial of

a physical activity programme to improve their symptoms of depression. The detailed sampling strategy of participants in the DeLLITE study is described elsewhere.[24,25] In brief, general practitioners invited all their patients aged 75+ to participate using a letter and a three-question screen for depression[26] to identify those with depressive symptoms. Those who were 'screened' as having depressive symptoms (two or more positive questions about depression), and who were interested, were visited at home to obtain written informed consent and to complete initial data collection.

Data collection

Trained research nurses used standardised structured questionnaires to ascertain demographic, health and social information from the participants. Age and gender and comorbidities, including cardiovascular disease, arthritis, history of syncope and/or falls, and a previous history of depression were determined during the interview. The severity of the depressive symptoms was established using the Geriatric Depression Scale (GDS), and was categorised according to standard criterion cut-off scores into 'without significant depressive symptoms' (score of 0 to 4) or 'with significant depressive symptoms' (score of 5 and above).[27] Full clinical data regarding the severity of the medical conditions or prior treatments was not available. Research nurses viewed all medications at the participants' home and recorded medication name, strength and frequency from the bottles/packs and/or blister packs. Over-the-counter products and complementary supplements used were also recorded. All medications were coded by therapeutic class, utilising the ATCC (Anatomical Therapeutic Chemical Classification) system developed by the World Health Organization (WHO) Collaborating Centre for Drug Statistics Methodology.[28]

Assessment of appropriateness of medication

Both the condition-dependent and condition-independent lists of the Beers' Criteria—adapted to the current product availability in NZ—were used to assess the appropriateness of medications used in the population sampled. The use of medications in NZ is guided by the Pharmaceutical Management Agency (PHARMAC), a government agency setting a formulary of publicly subsidised drugs. Access to the more expensive medications may be guided by an additional authority, which involves applying to a central body using set criteria. Medications that were not registered for use in NZ (at the time of the review in 2008) were omitted from both lists of the Beers' Criteria (e.g. meprobamate and ticlopidine) but medications that were registered for use but not subsidised by PHARMAC were included (e.g. chlorpropamide). Details of the drugs included in the lists can be found in the appendices in the web version of this paper. In the condition-dependent criteria, available medications that are used in NZ were incorporated into the list (shown in Appendix 1 in italics).

As not all the health problems experienced by the study population were listed in the original Beers' Criteria, the medical conditions in the condition-dependent list were expanded to accommodate some of the medical comorbidities reported by the DeLLITE participants (Appendix 2, medical conditions in italics).

Herbal and complementary medications were not assessed. All prescription items were assessed based on the adapted version of the Beers' Criteria (Appendices 1 and 2).

Data analysis

Participant data was entered into IBM SPSS statistical package (version 19). Frequencies, such as the number of participants on potentially inappropriate medications (PIMs) according to age, gender and depression scores were calculated. The association between inappropriate medication use and depression scores was assessed using the Chi-square statistic and logistic regression analysis to control for age, gender and comorbidities.

Results

Participant characteristics

A total of 353 individuals were eligible for the DeLLITE study, of which 193 were enrolled as participants.[25] Only those with complete medication data were eligible for inclusion in the present

study (n=191). Participants were predominantly women (59%) and had a mean age of 81 (standard deviation [SD] 4.3) years. The majority of medical conditions reported by the participants included cardiovascular disease (24%), arthritis (22%), history of syncope and/or falls (17%), and a previous history of depression (15%). Of the 191 participants, 55 (29%) had a GDS score of five or higher (significant depressive symptoms) and 56% of these participants were female. The majority (62%) of the participants in this subgroup were over the age of 85 years.

A total of 1440 medications were used by the 191 participants, of which 1329 were prescription medications and 111 were over-the-counter products. Every participant was prescribed at least one medication with a median number of six and a range of 1–21 medications. Polypharmacy (defined as the simultaneous use of 10 or more regular prescription medications) was identified in 23% of the participants. Cardiovascular drugs were the most commonly prescribed, with 81% of participants taking at least one cardiovascular medication. Fifty-two per cent of the participants were prescribed at least one or more CNS (central nervous system) medications.

Table 1 shows that overall there were no significant differences in the participant characteristics amongst those who were versus those who were not using any PIMs. Ninety-three participants (49% of our study population) were prescribed at least one PIM and inappropriate use was associated with using a greater number of medications (mean 8.5 medications for those with at least one inappropriate medication used vs 5.7, t 5.5 p<0.001).

Potentially inappropriate medications

Almost half (49%) of the participants were prescribed at least one potentially inappropriate medication. As presented in Table 2, a total of 134 PIMs were identified using the modified Beers' Criteria (either condition-dependent or condition-independent), of which 53 (40%) were CNS medications, namely amitriptyline (23%), dextropropoxyphene (17%), fluoxetine (11%), dothiepin (11%) and diazepam (7%). The most commonly prescribed potentially inappropriate medications were amitriptyline, dextropropoxyphene, quinine and benzodiazepines. The majority of amitriptyline prescribed was low-dose (i.e. 10 mg daily). Of the benzodiazepines, 55% were prescribed above the recommended dose range suggested by the Beers' Criteria. The second most commonly prescribed PIMs were those acting on the musculoskeletal system (16%), namely quinine (57%), naproxen (24%) and diclofenac (>100 mg daily; 9.5%). There were more participants on inappropriate medications according to the condition-independent list than according to the condition-dependent list of the Beers' Criteria (36% versus 26%; see Table 3).

The proportion of participants taking at least one PIM according to the condition-independent list was 35% (n=70), with 76% (n=56) of these medications considered high severity. The proportion of participants on inappropriate medication according to the condition-dependent list was 26%.

Table 1. Use of inappropriate medication according to the Beers' Criteria in older community-dwelling people with depressive symptoms

		No inappropriate use (n=98)	At least one inappropriate use (n=93)	Total (N=191)
Age: mean (SD)		81.2 (4.3)	81.0 (4.5)	81.1 (4.3)
Female: n (%)		57 (58)	56 (60)	113 (59)
GDS score: n (%)	0–4	70 (71)	66 (71)	136 (71)
	≥5	28 (29)	27 (29)	55 (29)
Total medications		5.7 (3.0)	8.5 (3.8)*	7.0 (3.6)

GDS Geriatric Depression Scale

* t 5.5 p<0.001

Table 2. Therapeutic medication use and inappropriate medication use in subgroups with and without significant depressive symptoms as assessed by the Geriatric Depression Scale (N=191 participants)

Therapeutic classes of medications outlined in Beers' Criteria (n=1329)	Any use (n=273)	Frequency of inappropriate use of medication		
		Total (n=134)	Subgroup with GDS ≥5 (n=44)	Subgroup with GDS <5 (n=90)
Cardiovascular (n=414)		20	7	13
Doxazosin	5	5	3	2
Amiodarone	4	4	0	4
Digoxin (≥ 0.125 mg)	9	4	2	2
Metoprolol*	46	3	0	3
Nifedipine	5	3	2	1
Atenolol*	15	1	0	1
Musculoskeletal (n=105)		21	7	14
Quinine*	14	12	4	8
Naproxen	5	5	2	3
Diclofenac (≥100 mg)†	8	2	1	1
Alendronate*	23	1	0	1
Sulindac	1	1	0	1
Central nervous system (n=226)		53	15	38
Central nervous system (excluding paracetamol) (n=164)		53	15	38
Amitriptyline†	12	12	1	11
Dextropropoxyphene (with paracetamol preparation)	9	9	4	5
Fluoxetine, daily	6	6	3	3
Dothiepin†	6	6	0	6
Diazepam †	4	4	1	3
Triazolam ≥ 0.250 mg)	12	4	2	2
Oxazepam*	8	4	0	4
Temazepam†	5	2	1	1
Nortriptyline*	6	1	0	1
Lorazepam*	4	1	1	0
Clonazepam*	2	1	1	0
Valporic acid *	2	1	0	1
Phenobarbitone (not indicated for epilepsy)	1	1	1	0
Doxepin†	1	1	0	1
Anti-infective (n=1)		1	0	1
Nitrofurantoin	1	1	0	1
Alimentary tract and metabolism (n=275)		16	6	10
Docusate/senna, regularly	17	8	3	5
Antacid*	6	6	2	4
Dicycloverine	1	1	0	1
Bisacodyl	1	1	1	0
Blood and blood forming (n=150)		16	5	11
Dipyridamole	9	9	3	6
Aspirin 300 mg*	18	7	2	5
Respiratory (n=74)		2	1	1
Promethazine	2	2	1	1
Genitourinary (n=18)		5	3	2
Oxybutynin	5	5	3	2
Anti-neoplastic and immunomodulating (n=4)		0	0	0
Dermatological (n=13)		0	0	0
Sensory (n=23)		0	0	0
Systemic—hormonal (n=13)		0	0	0
Various—nutrition (n=2)		0	0	0

GDS Geriatric Depression Scale
* Medications sourced solely from condition-dependent list
† Medications sourced from both condition-independent and condition-dependent lists

Table 3. Inappropriate use of medication according to the Beers' Criteria in those with and without depressive symptoms

a. Condition–dependent list

Inappropriate use of medications	Participants n (%)	Depressive status n (%)	
		GDS ≥5 (n=55)	GDS <5 (n=136)
One	41 (21)	10 (18)	31 (23)
Two	4 (2.1)	1 (1.8)	3 (2.2)
Three	2 (1.0)	–	2 (1.5)
Four	3 (1.6)	1(1.8)	2 (1.5)
Total	50 (25.7)	12 (21.6)	38 (28.2)

b. Condition–independent list

Inappropriate use of medications	Participants n (%)	Depressive status n (%)	
		GDS ≥5 (n=55)	GDS <5 (n=136)
One	54 (28)	16 (29)	38 (28)
Two	14 (7.2)	5 (9)	9 (6.6)
Three	2 (1.0)	2 (3.6)	–
Total	70 (36)	23 (42)	47 (35)

GDS Geriatric Depression Scale

When inappropriate use was compared between those with significant depressive symptoms (GDS ≥5) and those without (GDS <5), there were no significant differences observed (27 of 55 participants [49%] in the subgroup with significant depressive symptoms compared with 66 of 136 participants [49%] in the subgroup without significant depressive symptoms [Chi-square 0.005, p=0.54]. The association between inappropriate medication use, controlling for age, gender and other comorbidities, and significant depressive symptoms was also assessed using logistic regression analysis. Again, no significant correlates were found.

Discussion

The results of our study showed a high prevalence (49%) of inappropriate medication use in a sample of older people in primary care selected for a study because of depressive symptoms. When enrolled in the study and assessed, the subgroup with significant depressive symptoms (those with a GDS score ≥5), had no more inappropriate medication use than those with a GDS score <5. The mean number of medications per participant was 7 (SD 3.6), with those using PIMs taking more medications (8.5 vs 5.7). Slightly lower rates of inappropriate use have been found in other studies, with reported incidences between 14 and 32% of older participants in home care facilities and nursing homes taking at least one inappropriate medication.[11,20,29–31] A study by Baker et al.[32] examining inappropriate medication use in older adults with mental illness using the modified version of Beers' Criteria 2003 found that of 153 older adults (mean age 76 years old, range 52–95 years), 30.7% (47/253) were receiving at least one inappropriate medication. Only the condition-independent list had been applied in Baker's audit. The most commonly prescribed inappropriate medications were diazepam, ferrous sulfate, temazepam and lorazepam. Despite similar population demographics, Baker et al. had omitted the utilisation of the condition-dependent list completely in determining appropriate medication use. The partial utilisation of Beers' Criteria may underestimate the level of inappropriate prescribing in an older population where multiple comorbidities often coexist. Although not conclusive due to the limited number of comparable studies, the full utilisation of Beers' Criteria (both condition-independent and condition-dependent lists) could have contributed to the higher rate observed in our study population. The DeLLITE sample was chosen as a source of study participants because many people in that sample had shown depressive symptoms and many of the

antidepressants in use were deemed inappropriate according to the Beers' Criteria. The inappropriate medications with the most frequent occurrence found were amitriptyline (23%), fluoxetine (11%), and dothiepin (11%).

Age is one of the most influential factors in determining appropriate prescribing; however, age was not related to inappropriate use in this sample (not significant in the regression analysis). The study participants were 75 years or over, older than those in other studies[10,15,19] and inter-individual variability in health, disease and disability increases substantially with age. Furthermore, various health care settings studied and the use of different versions of the Beers' Criteria in other studies may be factors in contributing to the higher prevalence of inappropriate medication use observed in our population. Lastly, one of our hypotheses for the high level of inappropriate prescribing in this group of individuals may be because our study sample all had depressive symptoms at enrolment and depression is recognised as being related to increased medication use.[23] Our study did not show that those with significant depressive symptoms (i.e. GDS ≥5) were using potentially inappropriate medications significantly differently from those with GDS scores within the normal range. However, the sample studied had a high prevalence of depressive symptoms by design, and thus would be expected to be different than a general population sample of older people.

The Beers' Criteria are limited in assessing medication appropriateness. As purely explicit criteria, they do not allow for clinical judgment. For example, the majority of the amitriptyline doses reported in our study population are considered low for an antidepressant indication (i.e. 10 mg nocte), but may be adequate for neuropathic pain or urinary incontinence. Low dose tricyclic antidepressants (TCA), such as amitriptyline, may be the first-line choice for managing neuropathic pain. However, the Beers' Criteria consider any use of amitriptyline as inappropriate, even if used at lower doses. Other examples include amiodarone and doxazosin. Both were commonly prescribed in our sample population and in some situations are the only effective medications. Furthermore, Beers' Criteria has strict, and to some extent inflexible, criteria that label certain medication use as inappropriate even in situations where it may be the only effective treatment. Anxiety is one of the most difficult clinical mental health conditions to manage and is often non-responsive to single antidepressant management, requiring the initial use of benzodiazepines to effectively control the associated symptoms while awaiting a response to the antidepressant. The rate of inappropriate use of medications in this study may be, therefore, over-estimated and other studies are needed linking Beers' Criteria recommendations to outcomes from medications to further assess the suitability and generalisability of the Beers' Criteria in the mental health population.

In 2012, a new version of the Beers' Criteria was developed in collaboration with the American Geriatrics Society. Although the Beers' Criteria 2012 was not used in our study, it is interesting to find that this new version has addressed several of the limitations we found with the older version.

The new version has removed medications that are no longer available and added in drugs introduced since 2003. Notable new inclusions are thiazolidinediones or glitazones for those with heart failure, acetylcholinesterase inhibitors for those with a history of syncope, and selective serotonin reuptake inhibitors in the context of patient falls and fractures. The new criteria have included ratings of the quality of the evidence supporting the panel's recommendations. This may allow a more evidence-based application of the criteria.

It has been consistently reported that the Beers' Criteria should not substitute clinical judgment or the individualised decision-making process that must take place in consultation with patients and their caregivers. The criteria should primarily be used to guide interventions and identify individuals for comprehensive medication review, rather than merely as identifying specific targets for discontinuation.

In selecting the most suitable medication for this age group, clinical knowledge should guide

application of evidence-based knowledge. While use of Beers' Criteria may not aid prescribing decisions, it has the potential to 'red-flag' problematic drugs using its explicit criteria to signal involvement of the multidisciplinary team (i.e. specialists and pharmacists) to assist with the prescribing process in complex populations. In general, the following points remain sensible advice on prescribing for older people:

- avoid medication with high anticholinergic side effects;
- start with the lowest dose with titration to effect;
- aim for disease modification rather than treating symptoms; and
- avoid short-acting sedative hypnotics.

Managing mental health problems appropriately may mean use of medications on the Beers' Criteria list is necessary.

Study limitations

This research was conducted in a relatively small sample and thus generalisability to a large sample is unlikely. All study participants were recruited from general practices in central Auckland and were selected specifically as they scored 2 or more on the three-question depression screening tool, which means results may be more pertinent to those with some depressive symptoms. This group with depressive symptoms would be expected to have a different medication profile than a general community sample. Secondly, the use of the Beers' Criteria 2003 is based on consensus only. The use of the most updated Beers' Criteria 2012, which is both consensus based and evidence based, may result in more confidence in applying explicit criteria and instituting risk mitigation to avoid potentially inappropriate medication use. Finally, the comorbidities identified in study participants were not always available as specifically listed conditions in the Beers' Criteria condition-dependent list. For example, asthma/COPD is the condition listed in the condition-dependent list, whereas the patient's diagnosis was bronchiectasis. Better clinical correlation is needed when using any medication quality assessment process and this study is limited by not having access to adequate clinical information.

Conclusion

Almost half of our study population were receiving at least one inappropriate medication as per the modified Beers' Criteria used in this study, and clinical correlation was needed to truly decide if medication was inappropriate. No differences were observed in inappropriate medication use between those with and without significant depressive symptoms according to GDS score. Ongoing research to examine outcomes related to this medication use is needed. In the meantime, increased awareness of prescribing options is recommended.

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COMPETING INTERESTS
None declared.

APPENDIX 1: Adapted Beers' Criteria: Condition-independent list

Drug Class	Drug names/doses if specified	Severity	Comments
Long-acting benzodiazepines (BZD)	• Diazepam	High	These agents have very long half-lives, cause prolonged sedation and increase the risk of falls and fractures. If BZD therapy is unavoidable, use short-acting agents.
Short-acting BZDs, should rarely exceed the dose listed	• Lorazepam (3 mg) • Oxazepam (60 mg) • Triazolam (0.25 mg) • Temazepam (15 mg)	High	With rare exceptions, the agents should be used only in persons who are physically dependent or who are being treated with short-course therapy for an acute condition.
Barbiturates except phenobarbital for seizures		High	All use should be avoided except in individuals who are physically dependent or for seizure disorder management. There are safer sedative-hypnotics available.
	• Amitriptyline • Doxepin	High	Amitriptyline and doxepin are very sedating and anticholinergic—their use should be avoided.
	• Methyldopa • Methyldopa-hydrochlorothiazide	High	All use should be avoided. Methyldopa causes bradycardia and can exacerbate depression in the elderly. Safer antihypertensives are available.
	• Propoxyphene (Paradex®)	Low	All use should be avoided; it has little advantage over acetaminophen. Other analgesics are safer and more effective.
	• Diphenhydramine (Unisom®)	High	Use only in the smallest effective dose (50 mg daily at night maximum, no more than 7 days) and only for emergency treatment of allergic reactions. Causes confusion and sedation.
Anticholinergics and antihistamines	• Chlorpheniramine (Histafen®) • Diphenhydramine (Unisom®) • Hydroxyzine (Serecid®) • Promethazine (Phenergan®, Allersooth®) • Dexchlorpheniramine (Polaramine®)	High	All non-prescription and many prescription antihistamines can have potent anticholinergic effects and cause confusion and sedation. To treat allergic reactions, use non-anticholinergic antihistamines rather than these agents.
	• Dipyridamole	Low	Short-acting form may cause orthostatic hypotension. Long-acting form may be appropriate in persons who have artificial heart valves. Dipyridamole SR is considered appropriate while dipyridamole short-acting is not.
	• Digoxin	Low	Doses should not exceed 0.125 mg/day except when treating artificial arrhythmias. Diminished renal clearance increases risk for toxicity.
	• Ferrous sulphate >325 mg/day	High	Higher doses do not substantially increase iron absorption but do cause increased constipation.
Muscle relaxant anti-spasmodics	• Oxybutynin	High	The doses needed to achieve a therapeutic effect generally produce anticholinergic side effects poorly tolerated by the elderly.
Non-COX selective NSAID (long-term use of full doses)	• Naproxen • Ketorolac • Indomethacin	High	Potential for renal failure, gastrointestinal bleeding, hypertension and heart failure.
	• Daily fluoxetine	High	Has a long half-life and can produce insomnia and agitation. Safer alternatives exist.
Long-term use of stimulant laxative	• Bisacodyl (Ducolax®)	High	May be appropriate in the presence of opiate analgesic use. Otherwise, may exacerbate bowel dysfunction.

Drug Class	Drug names/doses if specified	Severity	Comments
	• Amiodarone	High	Associated with QT prolongation and torsades de pointes. Lack of efficacy in the elderly.
	• Nitrofurantoin	High	Potential for renal impairment; safer alternatives exist.
	• Doxazosin	Low	Potential for hypotension and dry mouth. Can exacerbate symptoms of stress incontinence and mixed-cause incontinence.
	• Short-acting nifedipine (Adalat 10®, Adalat 20®, Nyefax Retard®)	High	Potential for hypotension and constipation. Short-acting nifedipine means long-acting (as it is being compared with the extended release formulation).
Oral oestrogens	• Conjugated oestrogen (Premarin®)	Low	Carcinogenic effects (breast and endometrial cancer).
Gastrointestinal antispasmodics	• Dicyclomine (Merbentyl®) • Propantheline	High	All have uncertain effectiveness and are strongly anticholinergic. Avoid all use—particularly long-term use.
	• Disopyramide	High	Of all antiarrhythmic drugs, this is the most potent inotrope and therefore may induce heart failure in elderly patients. It is also strongly anticholinergic. Other antiarrhythmic drugs should be used.
	• Chlorpropamide	High	It has a prolonged half-life in elderly patients and could cause prolonged hypoglycaemia. Additionally, it is the only oral hypoglycaemic agent that causes SIADH (Syndrome of Inappropriate Antidiuretic Hormone).
	• Orphenadrine	High	Causes more sedation and anticholinergic adverse effects than safer alternatives.
	• Cimetidine	Low	CNS (central nervous system) adverse effects including confusion.
	• Clonidine	Low	Potential for orthostatic hypotension and CNS adverse effects.

Medications not included as not registered and unavailable in New Zealand

Independent of diagnosis

1. Pentazocine
2. Trimethobenzamide
3. Methocarbamol
4. Carisoprodol
5. Chlorzoxazone
6. Cyclobenzaprine
7. Metazalone
8. Chlordiazepoxide-amitriptyline
9. Perphenazine-amitriptyline
10. Meprobamate
11. Chlordiazepoxide
12. Clidinium-chlordiazepoxide
13. Halazepam
14. Chlorazepate
15. Reserpine
16. Dicyclomine
17. Cyproheptadine
18. Tripelennamine
19. Cyclandelate
20. Meperidine
21. Ticlopidine
22. Oxaprozin
23. Ethacrynic acid
24. Guanethidine
25. Isoxsuprine
26. Thioridazine
27. Mesoridazine

APPENDIX 2. Adapted Beers' Criteria: Condition-dependent list*

Medication	Disease or condition	Comments	Severity
High sodium content drugs (sodium and sodium salts [alginate bicarbonate, bisphosphate, citrate, phosphate, salicylate and sulphate]) • *Docusate sodium* • *Etidronate disodium* • *Phenytoin sodium* • *Aspro-Aspirin® (300 mg)* • *Quinine sulphate* • *Sodium valproate* • *Movicol®* • *Gaviscon®* • *Diclofenac sodium* • *Alendronate sodium*	Heart failure Hypertension *Heart attack/ angina* *Enlarged ventricle* *Aortic sclerosis*	Negative inotropic effect. Potential to promote fluid retention and exacerbate heart failure.	High
Aspirin >325 mg/day Non-selective NSAIDs • *Ibuprofen* • *Tenoxicam* • *Diclofenac* • *Naproxen* • *Indomethacin* • *Ketorolac* • *Meloxicam*	Gastric or duodenal ulcers *Gastric reflux*	May exacerbate existing ulcer disease or create new ulcers.	High
Clozapine Chlorpromazine *Pericyazine* Bupropion	Seizure control *Epilepsy*	These agents can lower the seizure threshold.	High
Aspirin NSAIDs • *Ibupofen* • *Ketorolac* • *Indomethacin* • *Tenoxicam* • *Diclofenac* • *Naproxen* • *Meloxicam* • *Coxibs* Dipyridamole Clopidogrel	Disorders of blood clotting (including anticoagulant therapy) • *Warfarin* • *Heparin*	Increased risk of bleeding through multiple mechanisms of action.	High

Medication	Disease or condition	Comments	Severity
Anticholinergics and antihistamines • *Chlorpheniramine* • *Diphenhydramine* • *Hydroxyzine* • *Promethazine* • *Dexchlorpheniramine* Gastrointestinal antispasmodics • *Dicyclomine* Muscle relaxants Oxybutynin Antidepressants • *Amitriptyline* • *Imipramine* • *Clomipramine* • *Fluoxetine* • *Citalopram* • *Paroxetine* • *Doxepin* • *Dothiepin* • *Nortriptyline* Decongestant (nasal sprays) Tolterodine	Bladder flow obstruction *Prostate problem* *Prostatectomy*	Can lead to urinary retention.	High
Alpha-blocker • Doxazosin • Terazosin • Prazosin Tricyclic antidepressants (TCA) • Imipramine • Doxepin • Amitriptyline • Dothiepin • Clomipramine Long-acting BZD • *Diazepam*	Stress incontinence	May worsen symptoms of incontinence.	High
TCA • Imipramine • Doxepin • Amitriptyline • Dothiepin	Arrhythmias *Atrial fibrillation* *Pacemaker*	Proarrhythmic potential.	High
Decongestant (nasal spray) Theophylline Methylphenidate Monoamine oxidase inhibitors (MAOIs)	Insomnia	CNS stimulant effects.	High
Metoclopramide Conventional antipsychotics • *Prochlorperazine* • *Pericyazine* • *Haloperidol* Barbiturates • *Phenobarbitone* Anticholinergics Oxybutynin	Parkinson's disease	Antidopaminergic and anticholinergic effects can worsen symptoms of parkinsonism.	High
Barbiturates Anticholinergics Antispasmodics Muscle relaxants CNS stimulants • Methylphenidate	Cognitive impairment *Neurological problems* *Dementia (Alzheimer's)*	CNS-altering effects can worsen cognitive performance.	High

Medication	Disease or condition	Comments	Severity
Long-acting BZD • *Diazepam* Sympatholytic agents • Methyldopa	Depression	May produce or exacerbate depression.	High
Methylphenidate Fluoxetine	Anorexia and malnutrition	These agents suppress appetite.	High
Short to intermediate BZD • *Temazepam* • *Oxazepam* • *Triazolam* • *Clonazepam* • *Nitrazepam* • *Lortazepam* • *Lorazepam* TCA • Imipramine • Doxepin • Amitriptyline • Dothiepin • Clomipramine	Syncope or fall *Hip Fracture/Broken bones* *Osteoporosis* *Collapse* *Vertigo* *Fainting attacks*	May produce ataxia, impair psychomotor function and increase falls.	High
SSRIs (selective serotonin reuptake inhibitors) • Fluoxetine • Citalopram • Paroxetine • Setraline	SIADH/Hyponatraemia	May exacerbate or cause SIADH	Low
Olanzapine	Obesity	May stimulate appetite and cause weight gain.	Low
Diazepam Beta-blockers • *Metoprolol* • *Celiprolol* • *Atenolol* • Propranolol • *Nadolol*	Chronic Obstructive Pulmonary Disease (COPD) *Asthma* *Emphysema* *Bronchiectasis*	CNS adverse effects. May induce respiratory depression. May exacerbate or cause respiratory depression.	High
Calcium channel blockers • *Amlodipine* • *Felodipine* • *Nifedipine* • *Verapamil* • *Diltiazem* TCAs • Imipramine • Doxepin • Amitriptyline • *Dothiepin* • *Clomipramine* Anticholinergics	Chronic constipation	May exacerbate constipation.	Low

Medications not included as not registered and unavailable in New Zealand

Considering Diagnosis

1. Phenylpropanolamine
2. Thioridazine
3. Thiothixene
4. Ticlopidine
5. Flovoxate
6. Tacrine
7. Pemolin
8. Detroamphetamine
9. Methamphetamine
10. Reserpine
11. Guanethidine
12. Fluvoxamine

* Italicised medical conditions are additions to include some of the medical comorbidities reported by DeLLITE study participants. Italicised drug names are additional medications that are used in New Zealand.