**Abstract:**

Aim
To investigate whether use of long acting benzodiazepines (BZs) by older people is mediated by physical or psychological factors.

Background
Two models explain older people’s benzodiazepine use, one physical and the other psychological.

Methods
Secondary analysis of data from a study of 1059 community-dwelling non-disabled people aged 65 years and over. Associations between demographic factors, health service use, and physical and psychological characteristics and benzodiazepine use were investigated.

Findings
The prevalence of benzodiazepine use in this sample was 3.3% (35/1059). In univariate analyses, benzodiazepine use was associated with female gender, low income, high consultation rates, polypharmacy, difficulties in instrumental activities of daily living, recent pain and psychological factors. In a multivariate analysis only two factors retained statistically significant independent associations with benzodiazepine use.
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<th>Response to Reviewers:</th>
<th>Our responses to the reviewer’s comments will be uploaded with the revised manuscript</th>
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<td>text</td>
<td>use: receiving only the state pension (OR = 4.0, 95% CI: 1.70, 9.80) and pain in the past 4 weeks (OR = 3.79, 95% CI: 1.36, 10.54).</td>
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</table>
Health risk appraisal in older people 7: Long acting Benzodiazepine use in community-dwelling older adults in London- is it related to physical or psychological factors?

Devoshree Chatterjee, Steve Iliffe, Kalpa Kharicha, Danielle Harari, Cameron Swift, Gerhard Gillman and Andreas E. Stuck
Health risk appraisal in older people 7: Long-acting Benzodiazepine use in community-dwelling older adults - is it related to physical or psychological factors?

ABSTRACT

Aim
To investigate whether the use of long-acting BZs, in individuals aged 65 and over is mediated by physical or psychological factors.

Background
Long-acting benzodiazepine (BZ) consumption among older people has implications for mortality, morbidity and cost-effective prescribing. Two models explain benzodiazepine use in this age group, one linked to physical illness and disability and one to psychological factors.

Methods
Secondary analysis of baseline data from a study of 1059 community-dwelling non-disabled people aged 65 years and over recruited from three general practices in London. For this analysis, use of long acting benzodiazepines was defined as any self-reported use of Diazepam or Nitrazepam in the last four weeks. Associations between demographic factors, health service use, and physical and psychological characteristics and benzodiazepine use were investigated.

Findings
The prevalence of benzodiazepine use in this sample was 3.3% (35/1059). In univariate analyses, benzodiazepine use was associated with female gender, low income, high consultation rates, physical factors (medication for arthritis or joint pain, polypharmacy, difficulties in instrumental activities of daily living, recent pain) and psychological factors (poor self-perceived health, social isolation, and symptoms of anxiety or agitation). In a multivariate logistic regression analysis only two factors retained statistically significant independent associations with benzodiazepine use: receiving only the state pension (OR = 4.0, 95% CI: 1.70, 9.80) and pain in the past 4 weeks (OR = 3.79, 95% CI: 1.36, 10.54).

Keywords: older people; benzodiazepines; pain; depression;
INTRODUCTION

In older people, use of long acting benzodiazepines are associated with multiple risks, including falls, drowsiness and ataxia, cognitive decline, impaired psychomotor function, and risk of dependence (Voyer et al 2010). Older adults tend to take long acting benzodiazepines for longer, risking accumulation and potentiation of their sedative side effects. The ageing population and polypharmacy with risks of adverse drug effects and drug induced iatrogenesis are contributing to increased demands on the UK National Health Service (NHS). Although long-term use of benzodiazepines has been discouraged now for some time (Leipzig et al 1999), their use continues to be a problem. Therefore, it is vital to ensure benzodiazepine drugs are prescribed appropriately, and for the shortest duration clinically indicated.


General practitioners managing older people are often faced with the dilemma of treating a symptom or seeking the underlying cause. Knowing more about the reasons behind the use of benzodiazepines by older adults may help develop more appropriate alternative management strategies. Two explanatory models of benzodiazepine use among older adults – the psychological and the physical described above - deserve further investigation. This study aimed to explore the prevalence and characteristics of long-acting benzodiazepine use in a cohort of community-dwelling patients aged 65 years and older and their relationships to the two models. We hypothesized that long-acting benzodiazepine use in the sample population would be associated with physical factors such as arthritis, difficulties in IADL, polypharmacy or pain, or with psychological factors such as depression, anxiety, poor self-perceived health, social isolation, and impaired memory. Following the epidemiological literature, we also hypothesised that female gender, lower educational attainment...
and increased service use would be positively associated with long-acting benzodiazepine use. Conversely, income above the state pension would have a protective effect.
METHODS

Three large group practices in suburban London were recruited to participate in a multi-centre, multinational randomised controlled trial investigating the effect of Health Risk Appraisal for Older persons (HRA-O) on health behaviours and status (Stuck et al 2002). Practices located in suburban London, particularly interested in primary care for older people, and using electronic medical recording systems in clinical encounters were purposively selected. A full account of the methodology of the study is available elsewhere (Stuck et al 2007), including practice size, recruitment of practices and patients, training of general practitioners in health promotion with older people, response rates, use of reminders and the evidence justifying the preventive care recommendations given. This study was part of a three nation RCT of health promotion for older people, and had data capture tools that reflected the consensus of opinion about salient clinical problems.

To identify eligible patients aged 65 years and over, practice lists were cleaned by general practitioners. Eligibility criteria were: those living at home, without a) evidence of need for human assistance in basic activities of daily living, b) high dependency due to major physical or psychiatric illness, or cognitive impairment, or c) a terminal illness. Patients also had to have a sufficient understanding of English to complete the questionnaires. This patient population was further characterised using the Probability of Recurrent Admissions (Pra) questionnaire (Pacala et al 1995), and asked to complete a consent form by post. The Pra measures risk of hospital admission, and stratifies the population by level of risk for future in-patient care. It was used in the main study as the basis for risk-stratified outcome and analyses.

Eligible and consenting patients were posted the HRA-O questionnaire. The HRA-O is a multidimensional, self-completion questionnaire collecting information on health, functional status, health behaviours, preventive care, and psychosocial factors in older people (Table 1). The development of the HRA-O questionnaire, the derivation of the instruments used in it, the exact definitions of the categories and the feasibility of its use in British primary care have been reported elsewhere (Iliffe et al 2005). Non-responders to the initial mailing were sent a postal reminder. Those who responded, and those who met the inclusion criteria described above, were included in the study. The findings reported in this paper are from the baseline completion of the questionnaire. We analysed data from participants who reported using two named long-acting benzodiazepines (Diazepam or Nitrazepam) in the preceding 4 weeks. Long acting benzodiazepines (rather than short-acting ones) were selected because of the high levels of risk associated with their use, including daytime sedation, cognitive and psychomotor impairment, increased risk of falls and fractures, and respiratory depression, particularly in older people (Mendelson 1992).
These two long-acting benzodiazepines were in common use in the UK at the time of data collection and are still prescribed today. Both the brand and generic names of the drug were included in the questionnaire.

At base-line, self-reported information on income (state pension only, versus more than state pension) was used as a measure of socio-economic status. Service use was recorded based on self-reported number visits to the doctor in prior 12 months.

The following physical characteristics were measured at base-line: assistance with more than one Lawton’s Instrumental Activities of Daily Living (Lawton & Brody 1969), polypharmacy (number of prescription medications) and physical activity by the Physical Activity Scale for the Elderly score (Washburn et al 1993). Pain experience was measured using the Geriatric Pain Measure, a 24-item multidimensional pain questionnaire that uses a 10-point modified Likert scale and also captures the impact of pain on everyday living (Ferrell et al 2000).

The following psychological factors were measured at base-line: social isolation was measured according to the Lubben Social Network Scale (Lubben et al 2006), and depressed mood was ascertained with the 5-item Mental Health Inventory Screening Test (MHI-5) (Sherbourne & Stewart 1999), one of the subscales of the Short Form-36 (SF-36), and asks questions about how the person felt during the past month. A score ≤ 65 indicated a depressed mood.

Data were analysed using SPSS (version 19) for Windows to carry out univariate and binary logistic regression analyses as appropriate. In the first stage, $\chi^2$ tests were used to explore the associations between any benzodiazepine use in the previous 4 weeks and the characteristics listed in Table 1. In the second stage of analysis, the variables significantly associated with the use of benzodiazepines in the previous 4 weeks were entered in a single forward step into a binary logistic regression model.
RESULTS

In all, 1059 patients aged 65 years and over were included across the three practices. Thirty five patients reported using a long-acting benzodiazepine (11 Nitrazipam, 24 Diazepam) in the preceding 4 weeks, a prevalence of 3.3% (35/1059). Table 1 shows the associations between the selected HRA-O domains and long-acting benzodiazepine use.

Table 1 near here

Long-acting benzodiazepine users were significantly more likely to be female (28, 80%). They were also more likely to have visited the doctor more than 6 times in the past year (21,60%) versus 14 ,47%), being in receipt of only the state pension (22,(62%) versus 13, 38%),and be taking medication for arthritis/joint pain ≥ 3 times/ week (15, 44% versus 7, 21%). No statistically significant differences were found in age or educational attainment.

Long-acting benzodiazepine users were significantly more likely to report needing help with instrumental activities of daily living (IADL) (63% versus 34%), have poorer self-perceived health (43% versus 21%), higher risk of social isolation (26% versus 14%), report pain in the previous four weeks (81% versus 39%), and scored lower on the mental mood screen (29% versus 13%). Six percent of benzodiazepine users stated they often or always experienced symptoms of depression or feeling low, compared to 2% of non benzodiazepine users. Three percent of patients using long-acting benzodiazepines stated they often or always experienced symptoms of anxiety or agitation, compared to 1.5% of non benzodiazepine users. Long-acting benzodiazepine users were more likely to have poorer self-perceived health (43% versus 21%), higher risk of social isolation (26% versus 14%), report pain in the previous four weeks (81% versus 39%), and scored lower on the mental mood screen (29% versus 13%). No difference was found according to cognitive impairment.

In multivariate analysis (see Table 1) only two factors remained significantly associated with use of long-acting benzodiazepines; higher socioeconomic status as determined by receiving more than solely the state pension, and pain in the past 4 weeks.
Discussion

The prevalence of use of Diazepam and Nitrazepam in this sample of older adults is 3.3%. Long-acting benzodiazepine use in this sample of older people is not independently associated with physical factors such as arthritis, difficulties in IADL or polypharmacy, or with psychological factors such as depression, anxiety, poor self-perceived health, social isolation, and impaired memory. It is independently associated with low income and pain, particularly pain which causes depressive symptoms.

The use of long-acting benzodiazepines in our sample population appears related to a socio-economic factor - pension level - and also to a physical symptom – pain. It raises the question whether in such cases treating the cause of pain in the form of pain-specific treatment approaches, would be more appropriate than using benzodiazepines.

Strengths and Limitations of the study

This was an in depth study of community dwelling older adults in an area which is surprisingly under-researched. However, the prevalence of patients using long-acting benzodiazepines in this community-dwelling was 3.3%, which is lower of that found in many (but not all) studies in other Western countries. The findings therefore need to be treated tentatively. This low prevalence may be attributable to the fact that long-term benzodiazepine use has been actively discouraged for some time now in the UK, particularly in older adults, and so represents a success story for general practice. It may also reflect the self-selected nature of the patients in the sample, who had joined a trial on health promotion, or self-selection by high-performing general practices with a special interest in health promotion in older people.

Secondly, due to the cross-sectional nature of the data, it is not possible to establish causality in the relationships between long-acting benzodiazepine use and the factors associated with it. Also, the number of cases and the number of variables in the statistical model may have resulted in the exclusion of some variables that would have been independently associated in a larger sample.

Third, there are some limitations related to the generalizability of the findings of this study to other populations. The sample was drawn from three general practices in suburban London with a predominantly white population, the results of which may differ from that of rural general practice patients, ethnic minorities or institutionalised patients. We cannot rule out a selection bias in recruitment of older people who may be more motivated to return lengthy questionnaires. The question related to long-acting benzodiazepine use covered only the preceding four weeks and thus, we may have missed patients who had recently discontinued, and we could not distinguish between short-term and long-term users. We did not have information on whether the prescription was
written by the patient’s GP, psychiatrist or other specialist, the dosage, quantity, time point in the course of long-acting benzodiazepine treatment and total duration prescribed, indications and proportion of medication used as regular and ‘as needed’ use. **Only the use of long acting benzodiazepines (diazepam and nitrazepam) was examined, and short acting benzodiazepines were not included.** Over against these limitations, the study had access to a relatively large sample size with homogeneity in many characteristics including age and background, and a high response rate, strengthening its internal validity.

**Comparison with existing literature**

Most other studies have included a wider range of benzodiazepines than we did. In 1999 in Ireland, Kirby et al. found prevalence rates of 17.3% for subjects of a similar age group to our study (Kirby et al 1999). A French study (Fourrier et al 2001) in 2001 revealed that 32% of its 2972 community dwelling subjects were using benzodiazepines at baseline. In Sweden, Johnell et al. in (2009) reported that 25% of patients aged 75 or over used one or more, and 5% used two or more benzodiazepines and benzodiazepine related drugs. More recently a Finnish study based on data collected from the population-based GeMS (Geriatric multidisciplinary strategy for the good care for the Elderly) project, analysed data from 700 participants aged 75 and over and found a baseline prevalence rate of 31% at baseline, of which 55% reported continued use in three further follow-ups (Rikala et al 2011). Our findings are consistent with those of population-based studies from several countries which suggest rates of benzodiazepine use range from 3 to 17% with rates typically higher among older than younger people (Cunningham et al 2010). In a study conducted in UK Primary care, De Wilde et al (2007) found that although 5.2% of older adults were still receiving benzodiazepines in 2003, prescription of benzodiazepines had fallen by a third from 79.3 per 1000 in 1994 to 52.4 per 1000 in 2003.

When Luijendijk et al.(2008) studied determinants of long-term benzodiazepine use, they found pain from joint disorders also increased the risk of long-term benzodiazepine use. People with lower socio-economic status receive a higher number of prescriptions than do those of higher socio-economic status (van Eijk et al 2010). Furthermore, Odubanjo et al (2004) compared the quality of prescribing between a primary care cohort of 66 521 relatively deprived and 28 534 affluent patients over 70 years old in Ireland and found a statistically significant higher percentage of the deprived cohort were prescribed a long acting benzodiazepine drug. This finding is consistent with the findings from our study.
Implications for future practice and research

Inappropriate use of benzodiazepines remains a concern, internationally (Campanelli 2012, Olfson 2015, Préville 2012). The findings of this study support the recommendation made elsewhere that primary care practitioners should enquire routinely about pain when seeing older adults in general practice (Carmaciu et al 2007). Good management of pain may avoid inappropriate use of long-acting benzodiazepines and reduce the risks of their associated morbidities. Future research could include analysis of a larger data set to explore further the relationship between pain and specific long-acting benzodiazepine use, and also explore the relationships between shorter-acting benzodiazepines (and newer equivalents) and pain.

Conclusion

A multidimensional approach to assessing and managing the circumstances and symptoms associated with potentially inappropriate benzodiazepine use appears justified in community-dwelling older people. Appropriate treatment of pain may further reduce the use of benzodiazepines in older patients.

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Ethics committee

Approval was obtained from Brent Medical Ethics Committee (BEC 745) and King’s College Hospital Research Ethics Committee (01–010)

Competing interests

The authors have stated that there are none

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References


Sherbourne CD, Stewart AL 1999: The MOS social support survey. Social Science and Medicine; 32, 705-714


### Table 1: Factors associated with use of long-acting benzodiazepines: univariate analysis and multivariate logistic regression analysis

<table>
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<tr>
<th>Factor</th>
<th>n (%)</th>
<th>Unadjusted OR</th>
<th>95% CI</th>
<th>p value</th>
<th>Adjusted OR</th>
<th>95% CI</th>
<th>p value</th>
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<td>Female n=583</td>
<td>28 (5.0)</td>
<td>3.380</td>
<td>1.463-7.809</td>
<td>0.003</td>
<td>2.003</td>
<td>0.684-5.861</td>
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<td>Male n=476</td>
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<td>Receives solely the state pension n=343</td>
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<td>1.706-6.993</td>
<td>0.001</td>
<td>4.081</td>
<td>1.698-9.804</td>
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<td>Receives more than state pension n=701</td>
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<td>Basic education only* n=629</td>
<td>16 (2.6)</td>
<td>0.597</td>
<td>0.301-1.185</td>
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<td>More than basic education n=424</td>
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<td>Age 75 or more n=463</td>
<td>20 (4.3)</td>
<td>1.749</td>
<td>0.885-3.454</td>
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<td>65-74 years old n=596</td>
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<td><strong>Service use</strong></td>
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<td>6 or more consultations in past 12/12 n=215</td>
<td>14 (6.5)</td>
<td>2.730</td>
<td>1.364-5.462</td>
<td>0.006</td>
<td>2.292</td>
<td>0.883-5.950</td>
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<td>Up to 5 consultations in past 12/12 n=823</td>
<td>21 2.6</td>
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<td><strong>Physical</strong></td>
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<td>Taking medicine for joint pain ≥3 times/week n=219</td>
<td>15 (6.8)</td>
<td>2.984</td>
<td>1.490-5.975</td>
<td>0.002</td>
<td>0.665</td>
<td>0.236-1.872</td>
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<td>Taking medicine for joint pain &lt;3 times/week n=790</td>
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<td>4 or more repeat prescription medications n=357</td>
<td>16 (4.5)</td>
<td>1.166</td>
<td>1.031-1.319</td>
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<td>Diagnosis of Arthritis/rheumatism n=430</td>
<td>19 (4.4)</td>
<td>1.965</td>
<td>0.974-3.963</td>
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<td>No diagnosis of arthritis/rheumatism n=609</td>
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<td>Difficulties in IADL n=361</td>
<td>20 (5.5)</td>
<td>3.182</td>
<td>1.537-6.587</td>
<td>0.002</td>
<td>1.888</td>
<td>0.739-4.821</td>
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<td>No IADL difficulties n=663</td>
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<td>Pain in past 4 weeks</td>
<td>25 (6.2)</td>
<td>6.544</td>
<td>2.660-16.103</td>
<td>&lt;0.001</td>
<td>3.787</td>
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<td>Symptoms of depression/feeling low n=116</td>
<td>10 (8.6)</td>
<td>1.525</td>
<td>1.153-2.017</td>
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<td>1.287</td>
<td>0.846-1.957</td>
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<td>Depression (Mental mood screen) N=150</td>
<td>10 (6.7)</td>
<td>2.622</td>
<td>1.232-5.581</td>
<td>0.01</td>
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<td>Negative mental mood screen n=888</td>
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<td>Fair or Poor self perceived health n=229</td>
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<td>2.814</td>
<td>1.417-5.590</td>
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<td>0.459-3.382</td>
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<td>Good or excellent self perceived health n=823</td>
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<td>Socially isolated n=146</td>
<td>9 (6.2)</td>
<td>2.213</td>
<td>1.016-4.824</td>
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<td>Not socially isolated n=902</td>
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<td>Symptoms of anxiety/agitation</td>
<td>16 (5.2)</td>
<td>1.440</td>
<td>1.065-1.947</td>
<td>0.02</td>
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<td>0.846-1.957</td>
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<td>Impaired memory  n=102</td>
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<td>0.845</td>
<td>0.254-2.809</td>
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<tr>
<td>No memory impairment n=921</td>
<td>32  (3.5)</td>
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IADL= Instrumental activities of daily living

* basic education only = left school at or before 16