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Health risk appraisal in older people 7: Long acting Benzodiazepine use in community-dwelling older adults - is it related to physical or psychological factors? --Manuscript Draft--

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Corresponding Author:	Steve Iliffe, FRCGP University College London London, London UNITED KINGDOM
Corresponding Author Secondary Information:	
Corresponding Author's Institution:	University College London
Corresponding Author's Secondary Institution:	
First Author:	Devoshree Chatterjee
First Author Secondary Information:	
Order of Authors:	Devoshree Chatterjee Steve Iliffe, FRCGP Kalpa Kharicha Danielle Harari Cameron Swift Gerhard Gillman Andreas Stuck
Order of Authors Secondary Information:	
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Abstract:	<p>Aim To investigate whether use of long acting benzodiazepines (BZs) by older people is mediated by physical or psychological factors.</p> <p>Background Two models explain older people's benzodiazepine, one physical and the other psychological.</p> <p>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.</p> <p>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</p>

	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).
Response to Reviewers:	Our responses to the reviewer's comments will be uploaded with the revised manuscript

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

1 Health risk appraisal in older people 7: Long-acting Benzodiazepine use in
2 community-dwelling older adults - is it related to physical or psychological
3 factors?

4 **ABSTRACT**

5 Aim

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

8

9 Background

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

13

14 Methods

15 Secondary analysis of baseline data from a study of 1059 community-dwelling non-disabled people
16 aged 65 years and over recruited from three general practices in London.

17 For this analysis, use of long acting benzodiazepines was defined as any self-reported use of

18 Diazepam or Nitrazepam in the last four weeks. Associations between demographic factors, health
19 service use, and physical and psychological characteristics and benzodiazepine use were
20 investigated .

21

22 Findings

23 The prevalence of benzodiazepine use in this sample was 3.3% (35/1059). In univariate analyses,
24 benzodiazepine use was associated with female gender, low income, high consultation rates,
25 physical factors (medication for arthritis or joint pain, polypharmacy, difficulties in instrumental
26 activities of daily living, recent pain) and psychological factors ((poor self-perceived health, social
27 isolation, and symptoms of anxiety or agitation). In a multivariate logistic regression analysis only
28 two factors retained statistically significant independent associations with benzodiazepine use:
29 receiving only the state pension (OR = 4.0, 95% CI: 1.70, 9.80) and pain in the past 4 weeks (OR =
30 3.79, 95% CI: 1.36, 10.54).

31

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

33

34

1 **INTRODUCTION**

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

11
12 Some epidemiological studies of benzodiazepine use in older adults suggest it reflects psychological
13 disorder including depression, suicidal ideation, panic disorder, anxiety, memory impairment,
14 poorer self-rated health and poorer life satisfaction (Kirby et al 1999, Balastrieri et al 2005, Stowell
15 et al 2008, Voyer et al 2009, Assem-Hilger et al 2009, Rikala et al 2011) , while others suggest it
16 reflects physical illness and disability such as coronary heart disease, hypertension, pain related joint
17 complaints, smoking, cancer, COPD, diabetes and multimorbidity (Dealberto et al 1997, Gleason et al
18 1998, Fourrier et al 2001, Luijendijk et al 2008, Cheng et al 2008, van Eijk et al 2010) . Most studies
19 show higher use in females(Kirby et al 1999, Jorm et al 2000, Windle et al 2007, Cheng et al 2008,
20 Fourrier et al 2001) but Mayer-Oakes et al.(1993) and Swartz et al.(1991) showed that use of
21 benzodiazepines was not associated independently with gender, but with physical health status,
22 which was poorer in women than men.

23
24 General practitioners managing older people are often faced with the dilemma of treating a
25 symptom or seeking the underlying cause. Knowing more about the reasons behind the use of
26 benzodiazepines by older adults may help develop more appropriate alternative management
27 strategies. Two explanatory models of benzodiazepine use among older adults – the psychological
28 and the physical described above - deserve further investigation. This study aimed to explore the
29 prevalence and characteristics of long-acting benzodiazepine use in a cohort of community-dwelling
30 patients aged 65 years and older and their relationships to the two models. We hypothesized that
31 long-acting benzodiazepine use in the sample population would be associated with physical factors
32 such as arthritis, difficulties in IADL, polypharmacy or pain, or with psychological factors such as
33 depression, anxiety, poor self-perceived health, social isolation, and impaired memory. Following the
34 epidemiological literature, we also hypothesised that female gender, lower educational attainment

1 and increased service use would be positively associated with long-acting benzodiazepine use.

2 Conversely, income above the state pension would have a protective effect.

3

4

1 **METHODS**

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

13

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

23

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

1 . These two long acting benzodiazepines were in common use in the UK at the time of data collection
2 and are still prescribed today. Both the brand and generic names of the drug were included in the
3 questionnaire.

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

7

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

14

15 The following psychological factors were measured at base-line: social isolation was measured
16 according to the Lubben Social Network Scale (Lubben et al 2006), and depressed mood was
17 ascertained with the 5-item Mental Health Inventory Screening Test (MHI-5) (Sherbourne & Stewart
18 1999), one of the subscales of the Short Form-36 (SF-36), and asks questions about how the person
19 felt during the past month. A score ≤ 65 indicated a depressed mood.

20

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

26

27

28

1 **RESULTS**

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

6
7 Table 1 near here

8
9 Long-acting benzodiazepine users were significantly more likely to be female (28, 80%). They were
10 also more likely to have visited the doctor more than 6 times in the past year (21,60%) versus 14
11 ,47%), being in receipt of only the state pension (22,(62%) versus 13, 38%),and be taking medication
12 for arthritis/joint pain ≥ 3 times/ week (15, 44% versus 7, 21%),. No statistically significant
13 differences were found in age or educational attainment.

14
15 Long-acting benzodiazepine users were significantly more likely to report needing help with
16 instrumental activities of daily living (IADL) (63% versus 34%), have poorer self-perceived health
17 (43% versus 21%), higher risk of social isolation (26% versus 14%), report pain in the previous four
18 weeks (81% versus 39%), and scored lower on the mental mood screen (29% versus 13%). Six
19 percent of benzodiazepine users stated they often or always experienced symptoms of depression or
20 feeling low, compared to 2% of non benzodiazepine users. Three percent of patients using long-
21 acting benzodiazepines stated they often or always experienced symptoms of anxiety or agitation,
22 compared to 1.5% of non benzodiazepine users. Long-acting benzodiazepine users were more likely
23 to have poorer self-perceived health (43% versus 21%), higher risk of social isolation (26% versus
24 14%), report pain in the previous four weeks (81% versus 39%), and scored lower on the mental
25 mood screen (29% versus 13%). No difference was found according to cognitive impairment.

26
27 In multivariate analysis (see Table 1) only two factors remained significantly associated with use of
28 long-acting benzodiazepines; higher socioeconomic status as determined by receiving more than
29 solely the state pension, and pain in the past 4 weeks.

30

1 **Discussion**

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

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

12

13 **Strengths and Limitations of the study**

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

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

27 Third, there are some limitations related to the generalizability of the findings of this study to other
28 populations. The sample was drawn from three general practices in suburban London with a
29 predominantly white population, the results of which may differ from that of rural general practice
30 patients, ethnic minorities or institutionalised patients. We cannot rule out a selection bias in
31 recruitment of older people who may be more motivated to return lengthy questionnaires. The
32 question related to long-acting benzodiazepine use covered only the preceding four weeks and thus,
33 we may have missed patients who had recently discontinued, and we could not distinguish between
34 short-term and long-term users. We did not have information on whether the prescription was

1 written by the patient's GP, psychiatrist or other specialist, the dosage, quantity, time point in the
2 course of long-acting benzodiazepine treatment and total duration prescribed, indications and
3 proportion of medication used as regular and 'as needed' use. **Only the use of long acting**
4 **benzodiazepines (diazepam and nitrazepam) was examined, and short acting benzodiazepines were**
5 **not included.** Over against these limitations, the study had access to a relatively large sample size
6 with homogeneity in many characteristics including age and background, and a high response rate,
7 strengthening its internal validity.

9 **Comparison with existing literature**

10 Most other studies have included a wider range of benzodiazepines than we did. In 1999 in Ireland,
11 Kirby et al. found prevalence rates of 17.3% for subjects of a similar age group to our study (Kirby et
12 al 1999). A French study (Fourrier et al 2001) in 2001 revealed that 32% of its 2972 community
13 dwelling subjects were using benzodiazepines at baseline. In Sweden, Johnell et al. in (2009)
14 reported that 25% of patients aged 75 or over used one or more, and 5% used two or more
15 benzodiazepines and benzodiazepine related drugs . More recently a Finnish study based on data
16 collected from the population-based GeMS (Geriatric multidisciplinary strategy for the good care for
17 the Elderly) project, analysed data from 700 participants aged 75 and over and found a baseline
18 prevalence rate of 31% at baseline, of which 55% reported continued use in three further follow-ups
19 (Rikala et al 2011). Our findings are consistent with those of population-based studies from several
20 countries which suggest rates of benzodiazepine use range from 3 to 17% with rates typically higher
21 among older than younger people (Cunningham et al 2010). In a study conducted in UK Primary care,
22 De Wilde et al (2007 found that although 5.2% of older adults were still receiving benzodiazepines in
23 2003, prescription of benzodiazepines had fallen by a third from 79.3 per 1000 in 1994 to 52.4 per
24 1000 in 2003.

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

1 **Implications for future practice and research**

2 Inappropriate use of benzodiazepines remains a concern, internationally (Campanelli 2012, Olsson
3 2015, Prévile 2012). The findings of this study support the recommendation made elsewhere that
4 primary care practitioners should enquire routinely about pain when seeing older adults in general
5 practice (Carmaciu et al 2007). Good management of pain may avoid inappropriate use of long-
6 acting benzodiazepines and reduce the risks of their associated morbidities. Future research could
7 include analysis of a larger data set to explore further the relationship between pain and specific
8 long-acting benzodiazepine use, and also explore the relationships between shorter-acting
9 benzodiazepines (and newer equivalents) and pain.

10

11 **Conclusion**

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

16

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22 **Ethics committee**

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24 Committee (BEC 745) and King's College Hospital
25 Research Ethics Committee (01-010)

26

27 **Competing interests**

28 The authors have stated that there are none

29

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32

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

Factor	n (%)	Unadjusted OR	95% CI	p value	Adjusted OR	95% CI	p value
Demographics							
Female n=583	28 (5.0)	3.380	1.463-7.809	0.003	2.003	0.684-5.861	0.20
Male n=476	7 (1.4)						
Receives solely the state pension n=343	21 (6.0)	3.448	1.706-6.993	0.001	4.081	1.698-9.804	0.002
Receives more than state pension n=701	13 (1.8)						
Basic education only* n=629	16 (2.6)	0.597	0.301-1.185	0.14			
More than basic education n=424	18 (4.2)						
Age 75 or more n=463	20 (4.3)	1.749	0.885-3.454	0.12			
65-74 years old n=596	15 (2.5)						
Service use							
6 or more consultations in past 12/12 n=215	14 (6.5)	2.730	1.364-5.462	0.006	2.292	0.883-5.950	0.09
Up to 5 consultations in past 12/12 n=823	21 (2.6)						
Physical							
Taking medicine for joint pain ≥ 3 times/week n=219	15 (6.8)	2.984	1.490-5.975	0.002	0.665	0.236-1.872	0.40
Taking medicine for joint pain < 3 times/week n=790	19 (2.4)						
4 or more repeat prescription medications n=357	16 (4.5)	1.166	1.031-1.319	0.01	1.028	0.852-1.240	0.77
Up to 3 repeat medications n=686	19 (2.8)						
Diagnosis of Arthritis/rheumatism n=430	19 (4.4)	1.965	0.974-3.963	0.06			
No diagnosis of arthritis/rheumatism n= 609	14 (2.3)						
Difficulties in IADL n=361	20 (5.5)	3.182	1.537-6.587	0.002	1.888	0.739-4.821	0.18
No IADL difficulties n=663	12 (1.8)						
Pain in past 4 weeks	25 (6.2)	6.544	2.660-16.103	<0.001	3.787	1.361-10.542	0.01
Psychological							
Symptoms of depression/feeling low n=116	10 (8.6)	1.525	1.153-2.017	0.003	1.287	0.846-1.957	0.24
No depression/low symptoms n= 907	23 (2.5)						
Depression (Mental mood screen) N=150	10 (6.7)	2.622	1.232-5.581	0.01	0.843	0.264-2.693	0.77
Negative mental mood screen n=888	24 (2.7)						
Fair or Poor self perceived health n=229	15 (6.6)	2.814	1.417-5.590	0.003	1.246	0.459-3.382	0.67
Good or excellent self perceived health n=823	20 (2.4)						
Socially isolated n=146	9 (6.2)	2.213	1.016-4.824	0.05	1.715	0.595-4.946	0.32
Not socially isolated n= 902	26 (2.9)						
Symptoms of anxiety/agitation	16 (5.2)	1.440	1.065-1.947	0.02	1.287	0.846-1.957	0.24

Impaired memory n=102	3 (2.9)	0.845	0.254-2.809	0.78			
No memory impairment n=921	32 (3.5)						

IADL= Instrumental activities of daily living

* basic education only = left school at or before 16