Determinants of Hypnotic Discontinuation One Month After Discharge from an Acute Geriatric Ward: A Prospective, Observational Study

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Abstract

Background

Deprescribing long-term hypnotic drug use is recommended in older adults to reduce medication-related harm such as falls. It is currently unknown whether this might be feasible in geriatric inpatients. The aim of this study was hence to determine predisposing factors for discontinuation of benzodiazepines and Z-drugs one month after discharge in geriatric inpatients receiving usual care.

Methods

A prospective observational study was performed at the University Hospitals Leuven (UZ Leuven, Belgium). Patient characteristics, hypnotic drug use and sleep quality were gathered up to one month after discharge. A multivariable logistic regression model was used to identify independent determinants.

Results

Chronic hypnotic drug use was highly prevalent (26.6%) in the geriatric population of UZ Leuven. Ninety-six patients with a mean age of 85.7 (SD 4.7) years admitted to the acute geriatric ward over a period of 10 months were included for analysis. Upon admission, 74% used a benzodiazepine and 26% a Z-drug. One month after discharge, 35 patients (36.5%) discontinued the hypnotic drug and in 23 cases (24.0%) the equivalent daily dose was reduced. Cessation of the hypnotic drug during hospitalization was found to be the only determinant influencing discontinuation one month after discharge with an odds ratio of 9.43 (95% confidence interval: 3.23 – 32.13). This was not associated with any deterioration of sleep quality.

Conclusions

This study confirms the overuse of long-term BZD and Z-drug use in geriatric patients. Cessation of hypnotic drugs during hospitalization was strongly associated with persistent discontinuation one month after discharge.

Trial registration

The study was approved by the Ethics Committee of UZ Leuven (registration number B322201629331).

Background

Insomnia and anxiety disorders are very common in daily clinical practice [1, 2]. First-line management largely consists of non-pharmacological approaches such as cognitive behavioral therapy [3–5]. Yet, hypnotic agents are still used very frequently. Clinical practice guidelines do not provide strong recommendations in support of their use due to limited efficacy and safety concerns [6, 7]. Efficacy is moderate at best and furthermore limited in time. A diminished response to the hypnotic and anxiolytic

effect of benzodiazepines (BZDs) is to be expected within the setting of days to weeks [8]. Tolerance to Z-drugs has been reported as well [9].

Prolonged BZD and Z-drug use has been associated with major adverse effects, such as cognitive impairment [10] and an increased risk of falling [11, 12]. Such iatrogenic harm can result in long term consequences, *e.g.* loss of independence and even death [13, 14]. Hypnotic drug use should hence be limited whenever possible to a maximum of four weeks [3–5]. Conversely, BZDs and Z-drugs are among the most prescribed psychotropic drugs and are frequently used to address these conditions [15–20]. In particular, long-term hypnotic drug use has been observed more frequently in older adults [20, 21]. Importantly, older adults are more prone to suffer from adverse effects, due to anatomical and physiological changes which may alter the pharmacokinetics and pharmacodynamics of hypnotic drugs [22].

BZD discontinuation has been shown to improve cognitive impairment associated with BZD use among older adults [23]. This is not self-evident as patients might incur withdrawal symptoms [24]. Several strategies to discontinue hypnotic drugs have already been investigated, including tapering the hypnotic drug dose, discontinuation of hypnotic drug use with pharmacological intervention, and discontinuation of hypnotic drug use with psychological support [24]. Petrovic *et al.* have shown in a small intervention study that short-term withdrawal during hospital stay might be safe and feasible [25].

No clear guidelines for hypnotic discontinuation are available and recommendations vary considerably, in particularly pertaining to the geriatric inpatient setting [8, 24]. We therefore aimed to perform a before-after study in which the intervention in the after-cohort would comprise a tapered discontinuation approach during hospital stay. In this paper we describe the data collected in the before-arm. We aimed to characterize discontinuation attempts in geriatric inpatients and sought to identify which determinants contributed to discontinuation one month after discharge. In addition, potential consequences of withdrawal on sleep quality were determined.

Methods

Setting and design

This prospective investigation concerned the pre-implementation cohort of an uncontrolled before-after study. It was carried out between October 2016 and August 2017 at the acute geriatric wards of the University Hospitals Leuven (UZ Leuven) in Leuven, Belgium. This study was observational and hence did not include any intervention, *i.e.* active cessation of hypnotic drug therapy. Treatment discontinuation was at the discretion of the treating geriatrician. Patients were only considered once for inclusion upon presentation. The study was approved by the Ethics Committee of UZ Leuven (registration number B322201629331).

Study participants

Patients were considered to be eligible for trial participation if the following criteria were met: admission to a geriatric ward with chronic BZD or Z-drug use, indication of the hypnotic drug being insomnia, anxiety or unknown and being at least 75 years old. Chronic BZD or Z-drug use was defined as administration at least five days a week for four or more consecutive weeks before admission. The patient or his representative was informed orally and written about the aims, benefits and potential drawbacks of participating in the study. Written informed consent needed to be provided, signed by the patient or his representative when the patient was unable to.

Exclusion criteria were defined as follows: not mastering the Dutch language, severe psychiatric or neurological disease (e.g. bipolar disorder, epilepsy or dystonia), end-of-life care, acute medical condition (according to the treating physician) which could preclude rapid discontinuation of hypnotic drugs during hospital stay, patients using a combination of BZDs and/or Z-drugs, discontinuation of the hypnotic drug before the patient could be included and planned discharge within three days. Dropouts were defined as patients who appeared not to meet inclusion criteria after enrollment.

Two groups were defined according to their hypnotic drug use one month after discharge: (A) patients who successfully discontinued hypnotic drug use and (B) patients who still used a hypnotic drug at that moment. Group B included both patients who never discontinued hypnotic drug use, as well as patients who relapsed.

Variables

Patient characteristics were obtained from the patient's electronic record upon enrollment. Following information was collected: age, gender, number of drugs on admission, presence of delirium in medical history, last reported mini-mental state examination (MMSE) score [26] and whether admission was caused by a fall (defined as no fall, fall without injury and fall with injury). Regarding hypnotic drug use the following was gathered: use of BZD or Z-drug, the actual molecule, indication, equivalent daily dose of lorazepam when a BZD was used, equivalent daily dose of zolpidem when a Z-drug was used and use of other hypnotic drugs (*e.g.* trazodone, mirtazapine or a barbiturate) [27, 28]. Sleep quality was assessed upon study enrolment using the Pittsburgh Sleep Quality Index (PSQI) [29]. The PSQI is a validated questionnaire to assess individual sleep quality based on 19 questions, divided into seven components. By weighing the score of each question of a component, the component score was obtained. The total score was the sum of the component scores and ranged from 0 to 21. High total scores corresponded to worse sleep quality. A total score greater than 5 indicated poor sleep [29].

One week after enrollment and at the moment of discharge from the acute geriatric ward, hypnotic drug use and residency of the patient was documented. In addition, at the moment of discharge, the length of stay (LOS) was documented and whether or not the patient had developed any acute delirium during hospitalization (based on entry in the electronic record by the treating physician). In the latter case, therapy to treat the delirium was documented as well. Two weeks after enrollment and one month after discharge, hypnotic drug use, residency of the patient and sleep quality were inquired.

The primary endpoint of this analysis was whether or not a BZD or Z-drug was used one month after discharge. Secondary endpoints were equivalent daily dose of the hypnotic drug and sleep quality one month after discharge.

Statistical analysis

Patients who completed the follow-up up to one month after discharge were included for analysis. Descriptive statistics were used to represent participant characteristics. Normally distributed variables were reported using means and standard deviations (SD). Non-normally distributed quantitative variables were reported using medians and interquartile range (IQR, represented as Q1-Q3). Qualitative variables were represented as n (%).

Sleep quality between participants of groups A and B at every time point was compared using the Mann-Whitney U test. Sleep quality within group A and group B over time was compared using the Friedman test.

Multivariable logistic regression analysis using backward elimination was performed to identify the independent predictors for hypnotic discontinuation one month after discharge. First, all independent variables were tested in a univariable analysis (UVA). Only significant variables ($p < 0.10$) were considered for the subsequent multivariable analysis (MVA). Variables with more than 5% missing values were discarded from further analysis. Multicollinearity was evaluated using the variance inflation factor. All statistical analyses were carried out using R version 3.6.2. Statistical significance was defined as $p < 0.05$ unless indicated otherwise.

Results

Study population

During the study period, 1550 patients were reviewed for eligibility and 412 (26.6%) chronically used a BZD or Z-drug for insomnia, anxiety or an unknown indication. Of all patients, 1350 did not meet inclusion criteria and 61 declined to participate. Two patients withdrew their informed consent, one patient was lost for follow-up and ten patients died, resulting in 96 patients included for analysis. Figure 1 depicts the patient flow through the study.

The mean age of the participants was 85.7 (SD 4.7) years and three quarters were female. The majority used a BZD (74%) and the main indication for hypnotic drug use was insomnia (88.5%). A discontinuation attempt during hospitalization was undertaken in 58.3% of the patients (n = 56). The median LOS on the geriatric ward was 12 (IQR 8–15) days during which ten participants (10.4%) developed a delirium. Patient characteristics are represented in Table 1.

Table 1
Patient characteristics.

Variable	All patients (n = 96)	Discontinued (n = 21)	Not discontinued (n = 75)
Age (years), mean (SD)	85.7 (4.7)	86.6 (4.7)	85.4 (4.7)
Sex, n (%)			
Male	24 (25.0)	5 (23.8)	19 (25.3)
Female	72 (75.0)	16 (76.2)	56 (74.7)
Number of drugs on admission, mean (SD)	9.6 (4.1)	8.2 (4.2)	10 (4.1)
Last reported MMSE, median (Q1-Q3)	24 (22–26)	26 (23–28)	24 (21.5–26)
Delirium in medical history, n (%)	8 (8.3)	2 (9.5)	6 (8.0)
Fall on admission, n (%)			
No fall	71 (74.0)	13 (61.9)	58 (77.3)
Fall without injury	8 (8.3)	2 (9.5)	6 (8.0)
Fall with injury	17 (17.7)	6 (28.6)	11 (14.7)
Indication for hypnotic drug use, n (%)			
Insomnia	85 (88.5)	20 (95.2)	65 (86.7)
Anxiety	7 (7.3)	1 (4.8)	6 (8.0)
Insomnia and anxiety	1 (1.0)	0 (0.0)	1 (1.3)
Unknown	3 (3.1)	0 (0.0)	3 (4.0)
Type of hypnotic drug, n (%)			
Benzodiazepine	71 (74.0)	15 (71.4)	56 (74.7)
Z-drug	25 (26.0)	6 (28.6)	19 (25.3)
Molecule, n (%)			
Alprazolam	7 (7.3)	1 (4.8)	6 (8.0)
Bromazepam	5 (5.2)	2 (9.5)	3 (4.0)
Clonazepam	1 (1.0)	0 (0.0)	1 (1.3)
Diazepam	2 (2.1)	1 (4.8)	1 (1.3)
Flunitrazepam	1 (1.0)	0 (0.0)	1 (1.3)

MMSE = mini-mental state examination, Q1-Q3 = interquartile range, SD = standard deviation.

Variable	All patients (n = 96)	Discontinued (n = 21)	Not discontinued (n = 75)
Flurazepam	1 (1.0)	1 (4.8)	0 (0.0)
Loprazolam	1 (1.0)	0 (0.0)	1 (1.3)
Lorazepam	30 (31.2)	6 (28.6)	24 (32.0)
Lormetazepam	20 (20.8)	2 (9.5)	18 (24.0)
Nitrazepam	1 (1.0)	0 (0.0)	1 (1.3)
Oxazepam	1 (1.0)	1 (4.8)	0 (0.0)
Prazepam	1 (1.0)	1 (4.8)	0 (0.0)
Zolpidem	24 (25.0)	5 (23.8)	19 (25.3)
Zopiclone	1 (1.0)	1 (4.8)	0 (0.0)
Equivalent daily dose of lorazepam on admission (mg), median (Q1-Q3)	2.5 (1.1-4.0)	1.7 (1.0–3.0)	2.9 (1.2-4.0)
Equivalent daily dose of zolpidem on admission (mg), median (Q1-Q3)	10.0 (5.0–10.0)	5.0 (5.0–10.0)	10.0 (5.0–10.0)
Use of other hypnotic drugs on admission, n (%)			
Use of trazodone	4 (4.2)	1 (4.8)	3 (4.0)
Use of mirtazapine	3 (3.1)	0 (0.0)	3 (4.0)
Discontinuation attempted upon enrollment, n (%)	56 (58.3)	12 (57.1)	44 (58.7)
Start of trazodone or mirtazapine during hospital stay, n (%)	5 (5.2)	3 (14.3)	2 (2.7)
Delirium during hospitalization, n (%)			
No delirium	86 (89.6)	16 (76.2)	70 (93.3)
Delirium without therapy	1 (1.0)	0 (0.0)	1 (1.3)
Delirium with hypnotic drug	2 (2.1)	1 (4.8)	1 (1.3)
Delirium with antipsychotic	6 (6.2)	4 (19.0)	2 (2.7)
Delirium with hypnotic drug and antipsychotic	1 (1.0)	0 (0.0)	1 (1.3)

MMSE = mini-mental state examination, Q1-Q3 = interquartile range, SD = standard deviation.

Variable	All patients (n = 96)	Discontinued (n = 21)	Not discontinued (n = 75)
Time to enrollment after admission (days), median (Q1-Q3)	2.5 (1–4)	3 (1–4)	2 (1–4)
Length of stay on geriatric ward (days), median (Q1-Q3)	12 (8–15)	14 (8–19)	11 (8–14)
MMSE = mini-mental state examination, Q1-Q3 = interquartile range, SD = standard deviation.			

Follow-up of the participants

Table 2 describes the follow-up of the participants. Sixty-six patients (68.8%) were still admitted to the geriatric ward seven days after enrollment, while 14 days after enrollment 23 patients (24%) were still hospitalized. Remaining patients were already discharged home or to a nursing home. Residency at other locations includes transfer to another hospitalization ward or medical rehabilitation center. Four and three patients were unavailable for follow-up seven days and 14 days after enrollment, respectively. One month after discharge, most of the patients were at home (57.3%) or living in a nursing home (32.3%). Three patients (3.1%) were readmitted to the geriatric ward.

Table 2
Follow-up of the participants.

	Upon enrollment	7 days after enrollment	14 days after enrollment	At discharge	1 month after discharge
Residency of the patient, n (%)					
Geriatric ward	96 (100.0)	66 (68.8)	23 (24.0)	96 (100.0)	3 (3.1)
Home	-	15 (15.6)	41 (42.7)	-	55 (57.3)
Nursing home	-	8 (8.3)	19 (19.8)	-	31 (32.3)
Other	-	3 (3.1)	10 (10.4)	-	7 (7.3)
Missing	-	4 (4.2)	3 (3.1)	-	0 (0.0)
Status of hypnotic use, n (%)					
Successful discontinuation attempt	-	27 (28.1)	25 (26.0)	35 (36.5)	21 (21.9)
Discontinued and relapsed	-	5 (5.2)	15 (15.6)	4 (4.2)	25 (26.0)
Never discontinued	-	60 (62.5)	53 (55.2)	57 (59.4)	50 (52.1)
Missing	-	4 (4.2)	3 (3.1)	-	-
Dose reduced compared to dose on admission, n (%)	-	28 (29.2)	22 (22.9)	32 (33.3)	23 (24.0)
Equivalent daily dose of lorazepam (mg), median (Q1-Q3)	2.5 (1.1-4.0)	1.7 (1.0–3.0)	2.0 (1.0–3.0)	1.7 (1.0–3.0)	2.4 (1.0–3.0)
Equivalent daily dose of zolpidem (mg), median (Q1-Q3)	10.0 (5.0–10.0)	5.0 (5.0–9.0)	5.0 (5.0–10.0)	5.0 (5.0–5.0)	10.0 (5.0–10.0)
Sleep quality					
PSQI completed by the participant	93 (96.9)	-	65 (67.7)	-	60 (62.5)
PSQI total score	8 (6.8–10)	-	7 (6–11)	-	8 (6–11)

PSQI = Pittsburgh Sleep Quality Index.

At discharge, 35 successful discontinuation attempts had been documented (36.5%). Four patients (4.2%) discontinued hypnotic drug use but relapsed during hospital stay. The equivalent daily dose of 32 patients (33.3%) was reduced at the moment of discharge in comparison with the equivalent daily dose on admission. One month after discharge, 21 patients (21.9%) had discontinued their hypnotic drug use,

while 75 patients (78.1%) were still using a BZD or Z-drug. The equivalent daily dose was reduced in 23 cases (24.0%). Two patients (2.1%) had switched from a BZD at baseline to a Z-drug one month after discharge.

The total PSQI score did not differ between group A and group B upon enrollment (p = 0.817), 14 days after enrollment (p = 0.282) or one month after discharge (p = 0.117). In addition, the total PSQI score did not differ significantly over time within group A and B either (p = 0.128 and p = 0.477, respectively).

Determinants of hypnotic discontinuation one month after discharge

Univariable logistic regression showed that 11 variables were associated with hypnotic discontinuation one month after discharge (Supplementary Table 1, Additional File 1). Following variables were excluded for analysis based on multicollinearity with other variables: hypnotic drug discontinued one week after enrollment, hypnotic drug discontinued two weeks after enrollment and antipsychotic in context of delirium. PSQI component 6 two weeks after enrollment and PSQI accomplished by the patient two weeks after enrollment were excluded due to too many missing values. Multivariable logistic regression showed that hypnotic discontinuation at discharge was the single significant independent predictor for hypnotic discontinuation one month after discharge (p < 0.001) with an odds ratio equal to 9.43 (95% CI 3.23–32.13) (Supplementary Table 2, Additional File 2).

Discussion

In our prospective, observational study we found a high prevalence of chronic hypnotic drug use, *i.e.* 26.6% of all patients admitted to the geriatric ward. We included 96 patients using a BZD or a Z-drug chronically. Hypnotic drug use was discontinued in 36.5% of the patients at discharge. A small minority of the patients (4.2%) discontinued but was relapsed at discharge, while many patients (26.0%) were relapsed one month after discharge. The main determinant for drug discontinuation at one month was deprescribing to have occurred during hospital stay. Of all participants, 21.9% successfully discontinued hypnotic drug use one month after discharge.

Previously reported estimates concerning long-term hypnotic drug use vary from 20% to more than 50%, depending on the age and residence of the study population, but this number has been decreasing over the past years [20, 21, 30–32]. The prevalence in our population (26.6%) is therefore rather low. Indeed, the true number of long-term hypnotic drug users might be an underestimation as patients who used multiple hypnotic drugs or had already discontinued were not considered for study participation.

Our findings on discontinuation were higher than owing to voluntary cessation in outpatient care due to the deprescribing culture among the physicians and awareness campaigns in the hospital. In a recent retrospective study performed in the United States, spontaneous discontinuation of chronic BZD use in adults aged 18 years and older was only 13.4% at the end of the following year which is much lower than

in our study [33]. The discontinuation rate of the control group in the EMPOWER trial was 5% [34]. A patient empowerment intervention in combination with a personalized tapering protocol, on the other hand, resulted in a BZD discontinuation rate of 27% demonstrating the added value of such an approach. However, this trial was performed in community-dwelling adults aged 65 and older who received little support, which might have mitigated the impact of the intervention [34].

Since the median LOS of the participants was 12 days, discontinuation was performed within a limited time window, indicating that short-term withdrawal might be feasible in the hospital setting. Our results showed that discontinuation of the hypnotic drug during hospitalization was strongly associated with discontinuation one month after discharge. This can be explained by the fact that discontinuation during hospitalization occurred under close monitoring of a physician and that patients were only discharged when they were considered to be clinically stable. Importantly, our results also showed that there was no difference in sleep quality between the two groups or within groups over time, demonstrating that hypnotic drug discontinuation was not associated with deterioration of sleep quality. In fact, overall sleep quality in the study population was poor, reflected by a median total PSQI score higher than 5 at all follow-up moments [29]. It was remarkable that two variables related to experiencing a delirium during hospitalization were significant in the UVA (*i.e.* abrupt discontinuation during hospitalization, delirium during hospitalization) but not in the MVA. These variables were expected to negatively contribute to hypnotic discontinuation one month after discharge. A possible explanation for this could be that insufficient participants experienced a delirium to significantly contribute to the hypnotic discontinuation rate.

A first major strength of our study was that we enrolled geriatric patients, including very old subjects. To our knowledge, this was the first study of this magnitude investigating hypnotic discontinuation in this subset of the geriatric population. Second, our definition of chronic hypnotic drug use was relatively short compared to previous reports [25, 35–37]. We deliberately chose this definition because guidelines specifically recommend to limit BZD or Z-drug use to maximally four weeks [38]. Third, the median MMSE of 55 out of the 96 participants was 24, which is considered to be the lower limit of normal cognition [39]. We were hence able to include a larger number of cognitively impaired older adults than in previous investigations, where cognitive impairment was frequently defined as an exclusion criterion [25].

Our study had some limitations as well. First, no blood or urine sampling was performed to establish actual discontinuation. After discharge, we relied on information provided by the participants or their relatives. Second, even though the PSQI is a validated questionnaire, it could be questioned whether it gives an accurate measurement of sleep quality. Polysomnographic sleep measurement would have been a more objective measure, but this was not feasible and might have impaired the willingness to participate [29]. Third, the Hawthorne effect may have played a role as well since participating to a study may influence the reported sleep quality by the participants [40]. Fourth, despite clearly stating in plain language that this was an observational study, a large number of patients were still anxious about their hypnotic drug being discontinued. There was also a substantial influence of family members who were convinced that participating in this study would be an additional burden for already fragile patients. We

hypothesize that this is one the major reasons why about one third of the patients eligible for enrollment refused to participate. Fifth, physicians already discontinued hypnotic drug use in 8.9% of the patients before the patient could be enrolled. In addition, when hypnotic drug use was not registered in the electronic record or when hypnotic discontinuation was performed at the emergency department, this was not taken into account. As a result, the true discontinuation rate might have been higher. Sixth, we attempted as much as possible to obtain information from the electronic record of the hospital or through other health-care professionals for non-hospitalized patients. Nevertheless, when patients were discharged home, we had to rely on information provided by the patient or his family, thereby possibly compromising the accuracy of the information. In addition, some information might not have been reliably documented in the electronic record such as whether or not the patient experienced a delirium during hospitalization. Seventh, some relevant variables were not documented and their contribution to hypnotic drug discontinuation could therefore not be investigated. For instance, an interesting variable would be the duration of hypnotic drug use before admission. However, we were unable to determine this variable with the required accuracy. Finally, we were unable to judge the long-term discontinuation rate (*e.g.* over 6 or 12 months), owing to the restrictions imposed by the Ethics Committee. They argued that the study might interfere too much in the relationship between patients and the primary care physicians. Nevertheless, the highest discontinuation rate was achieved three months after sending of a discontinuation letter [41]. About half of patients still relapsed thereafter, emphasizing the importance of a longer follow-up period.

An intervention to improve the discontinuation rate should focus on different aspects. Based on previous report, it might be beneficial to send a discontinuation letter to the patients' GP and family in addition to deprescribing hypnotics drugs during hospital stay [41]. In fact, the individual healthcare professional could be the most important contributing factor to hypnotic discontinuation underlining the importance of involving the patients' GP early on in the deprescribing process [33]. As the patient's family had a considerable influence on the decision to participate in this study, their importance should not be overestimated. They should be informed about the disadvantages of chronic hypnotic drug use and should be involved to encourage the patient when necessary. Because recommendations of ward-based clinical pharmacists are generally well-accepted by physicians [42], formulating a well-considered advice regarding hypnotic drug use to the geriatrician is expected to have an impact as well. All together, these findings illustrate that a multifaceted intervention should be implemented to maximize the success rate of hypnotic discontinuation one month after discharge, while focusing on discontinuation during hospital stay.

In the post-implementation cohort of this study we will therefore implement an intervention consisting of four components. First, a standardized withdrawal scheme will be implemented, based on the protocol of Petrovic *et al.* [25]. Second, educational and informational moments will be offered to the ward-based physicians and nursing staff. Third, patients will be informed about the side effects of hypnotic drugs and the possibility of worsening sleep in the first days after discontinuation of the hypnotic drug. Fourth, the patient's GP will be informed by phone and with a letter about the patient's study participation. For patients going to a nursing home, the nurses will be informed by phone as well.

Conclusions

This study confirms the overuse of long-term BZD and Z-drug use in geriatric patients. Geriatricians already ceased hypnotic drugs in a number of cases during hospital stay. This was not associated with deterioration of sleep quality, supporting the feasibility of discontinuation at short notice. Cessation of hypnotic drugs during hospitalization was strongly associated with persistent discontinuation one month after discharge.

List Of Abbreviations

BZD, benzodiazepine

GP, general practitioner

IQR, interquartile range

LOS, length of stay

MMSE, Mini-mental state examination

MVA, multivariable analysis

PSQI, Pittsburgh Sleep Quality Index

UVA, univariable analysis

Declarations

Ethics approval and consent to participate

The study was approved by the ethics committee of UZ Leuven (registration number B322201629331). Written informed consent was provided by all participants or their representative.

Consent for publication

Not applicable.

Availability of data and material

The dataset of the current study is available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

PVB, AL, JT and LVDL contributed to the design and performance of the study. All authors contributed to analyzing and interpretation of the results and to writing of this manuscript. PVB drafted the manuscript and managed suggestions and feedback of the other authors. All authors read and approved the final version.

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Figures

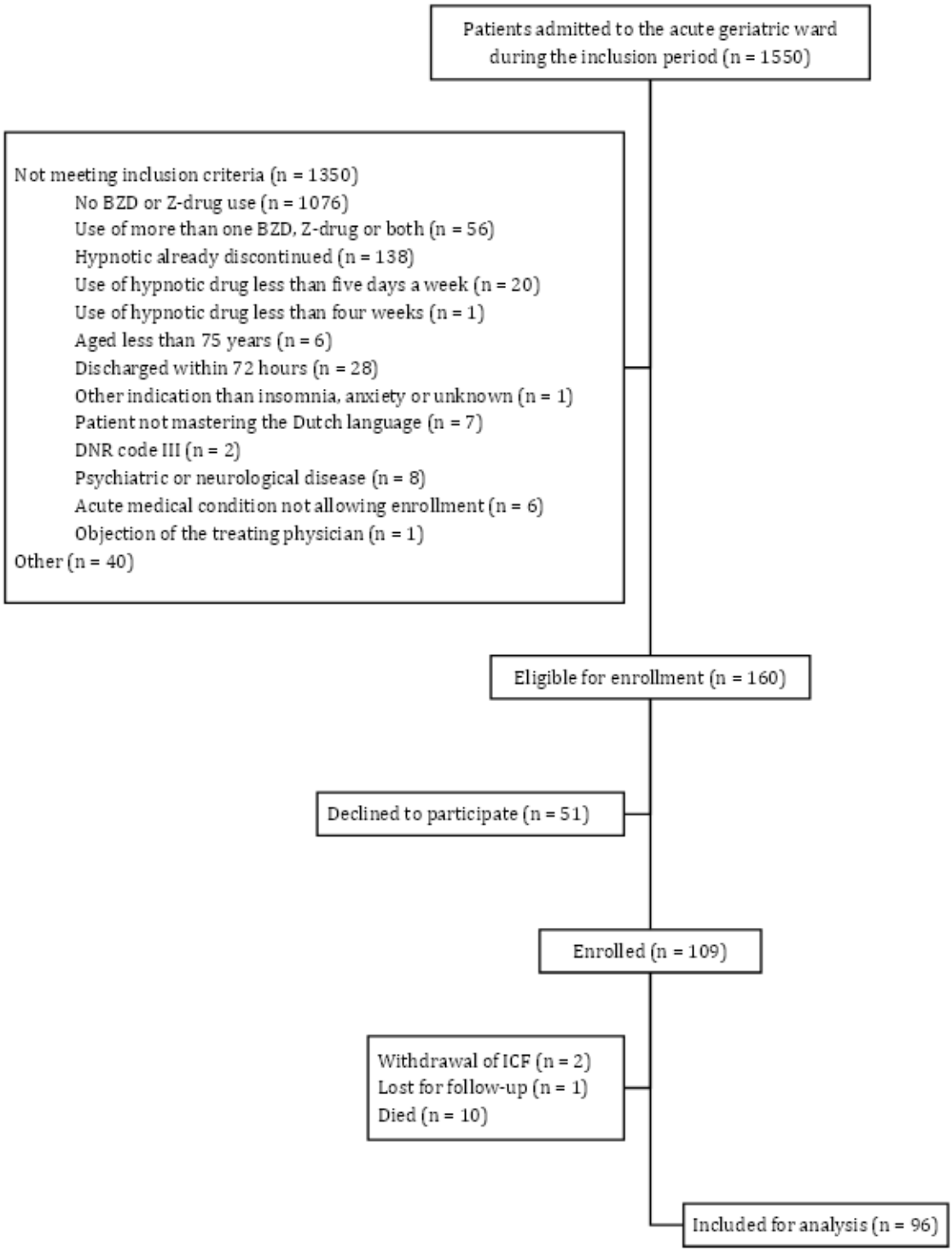

Figure 1

CONSORT diagram of patient flow through the study. BZD = benzodiazepine. DNR = Do Not Resuscitate. ICF = informed consent form.

Supplementary Files

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