Brief Intervention for Sleep Medication Misuse Among Elderly (BI-sleep)

Clinical trials reg: NCT06032715

Originally submitted Nov 7th, 2024

Resubmitted Nov 13th, 2024

(detailed analysis plan does not need to be passed by the Ethics board in Norway)

Analyses plan for main RCT

All outcome measures except on screening population (previously submitted) in registered protocol

STATISTICAL ANALYSIS PLAN

Design

The analyses will be split into two phases.

In phase one, four main outcomes, one primary – the proportion of participants without inappropriate z-hypnotics use (≥four weeks, ≥three times per week) and three secondary – sleep complaints, pain level and cognition) will be assessed at 6 weeks after baseline.

The outcomes will be compared between brief intervention (BI) and business as usual (BAU) groups by z-test for proportions for primary outcome and independent-samples t-test for secondary outcomes. Similar comparison of groups will also be performed 6 months later

In phase two, after 6 months from baseline, open cross-over from BAU to BI group will be offered, as phase two of the study. Those crossing over from BAU to BI will be provided the intervention. Six weeks after cross-over the groups will be compared in the same way as in phase one. Additionally, a comparison of groups will be performed at 6 months after cross-over.

Sample size

Primary outcome in this study is a proportion of patients with inappropriate use of Z-hypnotics (≥four weeks, ≥three times per week). We assumed that a proportion of patients who are no longer inappropriate users of Z-hypnotics at 6 weeks after baseline is 30% in BI and 2% in BAU group. To show that the difference between the groups is significant at 5% significance level with a power of 80% by using a z-test for proportions, the estimated number of patients was 26 in each group.

The additional power calculations for the secondary outcomes pain and cognition, while heavily dependent on the main outcome, was felt not to yield feasible numbers of recruited patients (e.g. n=192 per study arm), based on our previous experience with a similar study (Kristoffersen et al, JNNP, 2015). However, we decided to increase recruitment to a feasible range of 120 patients to be able to address also these secondary outcomes with a reasonable power, should the primary outcome give a higher proportion of patients successfully removed from inappropriate use. This larger sample will also allow adjustment for potential cluster effect on the GP level.

Primary analysis

As primary analysis, main outcome, the proportion of participants without inappropriate z-hypnotics use (≥four weeks, ≥three times per week), will be compared between BI and BAU groups at 6 weeks after baseline by a z-test for proportions.

Secondary analysis

Secondary analyses will include secondary outcomes including sleep complaints, pain and cognition assessed at 6 weeks, and primary and secondary outcomes assessed longitudinally. The groups will be compared by appropriate statistical tests. Z-test for proportions or independent samples t-test will be applied to compare groups at single time points. Generalized linear mixed models with random intercepts for patients will be estimated to assess differences in groups in trend in dichotomous or continuous outcomes. In the case of

considerable cluster effect on general practitioner (GP) level random intercepts for patients nested within GP will be included. The models will contain fixed effects for time dummies, group dummies and the interaction between these two.

Study population

Intention-to-treat analysis is a standard when analysing the data from a randomised controlled trial and will also be analysed here. However, as we experienced in an early stage of the study, some GPs randomised to BI arm dropped the first course, and thus their patients could not be provided the BI. Thus, intention-to-treat analysis is clearly compromised, which consequently implies that per-protocol analysis should be the main analysis strategy.

Qualitative analysis

We will, in a separate qualitative study, conduct a thematic analysis on group interviews with GPs that participated in the BI training course and study. The aim of this study is to understand the GPs experience and adherence of using BI tool, their perception of their patient's involvement and motivation. In addition to discussion about strategies for a large-scale implementing BI as an instrument to deprescribe inappropriate z-hypnotics.