BMJ Open

Course of fear of falling after hip fracture: findings from a 12-month inception cohort

Maaike N Scheffers-Barnhoorn, Miriam L Haaksma, Wilco P Achterberg, Arthur HP Niggebrugge, Max PL van der Sijp, Jolanda CM van Haastregt, Monica van Eijk

ABSTRACT

Objectives To examine the course of fear of falling (FoF) up to 1 year after hip fracture, including the effect of prefracture FoF on the course.

Design Observational cohort study with assessment of FoF at 6, 12 and 52 weeks after hip fracture.

Setting Haaglanden Medical Centre, the Netherlands.

Participants 444 community-dwelling adults aged 70 years and older, admitted to hospital with a hip fracture.

Main outcome measure Short Falls Efficacy Scale International (FES-I), with a cut-off score ≥11 to define elevated FoF levels.

Results Six weeks after hip fracture the study population-based mean FES-I was located around the cut-off value of 11, and levels decreased only marginally over time. One year after fracture almost one-third of the population had FoF (FES-I ≥11). Although the group with prefracture FoF (42.6%) had slightly elevated FES-I levels during the entire follow-up, the effect was not statistically significant. Patients with persistent FoF at 6 and 12 weeks after fracture (26.8%) had the highest FES-I levels, with a mean well above the cut-off value during the entire follow-up. For the majority of patients in this group, FoF is still present 1 year after fracture (84.9%).

Conclusions In this study population, representing patients in relative good health condition that are able to attend the outpatient follow-up at 6 and 12 weeks, FoF as defined by an FES-I score ≥11 was common within the first year after hip fracture. Patients with persistent FoF at 12 weeks have the highest FES-I levels in the first year after fracture, and for most of these patients the FoF remains. For timely identification of patients who may benefit from intervention, we recommend structural assessment of FoF in the first 12 weeks after fracture.

INTRODUCTION

Hip fracture, being one of the most serious fall-related injuries and representing the second most common fragility fracture in older adults, has a significant impact on the healthcare system. Despite extensive rehabilitation, a considerable number of patients experience permanent morbidity and disability, resulting in substantial costs in both (post)acute settings and long-term care.

Moreover, the expected rise in absolute numbers—up to 4 million in 2025, and over 6 million in 2050—will further contribute to the high economic burden and societal impact. To date, many prognostic factors have been identified. This includes fear of falling (FoF), defined as ‘a lasting concern about falling that leads to an individual avoiding activities that he/she remains capable of performing.’ Considering that FoF is common following hip fracture and has been found to impede functional recovery after fracture, this may be a meaningful factor to address in order to improve the recovery process.

Although various effective treatment programmes are available for community-dwelling older adults, studies evaluating treatment of FoF for patients with hip fracture are scarce, and their findings inconclusive. One possible explanation for the inconsistent findings is the timing of the intervention. To date, the interventions have been conducted mainly during inpatient rehabilitation, representing the early stage of recovery. However, associations between FoF and impaired

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study includes longitudinal follow-up assessments of fear of falling (FoF) in patients with hip fracture up to 1 year after hip fracture.

⇒ This study is based on a large inception cohort (without inclusion or exclusion criteria), increasing the generalisability of the results to the majority of patients with hip fracture.

⇒ The findings of this current study are based patients with an outpatient follow-up assessment at 6, and 12 weeks, and will therefore not be generalisable to patients with severe cognitive or physical impairment unable to attend the outpatient clinic.

⇒ In this study, the assessment of prefracture FoF may have been susceptible to recall bias due to the retrospective character.
functional recovery were found primarily for the period 6 weeks after fracture and beyond, not for the early stages after hip fracture (2–4 weeks). This may imply that FoF in the early stages of recovery is not a barrier to functional recovery under all circumstances. Insight into the course of FoF after hip fracture can provide a better understanding of the characteristics of FoF in this population, and help differentiate between patients with limited FoF, and those at risk for maladaptive FoF, that is, those forms of FoF that lead to impairment of physical activities and daily functioning. In turn, this may help identify patients who may benefit from intervention. However, at present, little is known about the clinical course of FoF after hip fracture, and the available data on this subject is limited by short follow-up.

In light of the above-mentioned knowledge gap, the objective of this study is to examine the course of FoF up to 1 year after fracture. This includes analysis of FoF trajectories for specific subgroups that could be relevant for clinical practice, such as patients who have experienced FoF prior to the hip fracture. However, the absence of prefracture FoF has been associated with successful short-term functional recovery, which points towards an important role for prefracture FoF in the recovery process. Although the mechanism for this effect remains to be determined, we expect that prefracture FoF has the potential to affect the course of FoF after fracture, and could therefore affect functional outcome. For this purpose, we will explore FoF trajectories based on the presence/absence of FoF prior to fracture. Furthermore, we will explore whether persistent FoF in the first 12 weeks (short term) is related to an increased risk for FoF 1 year after fracture.

METHODS
Study design, setting and patients
This is a longitudinal observational inception cohort study. All patients with a hip fracture admitted to the Haaglanden Medical Centre hospital, the Netherlands, in the period 1 January 2018 to 1 March 2020 were included in this inception cohort. All data were assessed as part of routine data collection for this target group. For this current study, we included all patients aged 70 years or older, who were community-dwelling prior to fracture (ie, not permanently residing in a nursing home or other residential care setting before admission), and for whom complete data was available for the covariates required for the analyses (see section ‘independent variables’ and figure 1).

Assessments
Data were collected at four fixed time points. Baseline data were collected during hospital admission. Follow-up assessments were conducted during the outpatient follow-up visits at 6, 12 and 52 weeks after fracture.

Primary outcome measure
FoF was measured with the Short Falls Efficacy Scale International (FES-I), administered during all three follow-up visits. The Short FES-I is a seven-item instrument, scored on a four-point Likert scale, assessing FoF related to basic physical and social activities. The total score on the Short FES-I ranges from 7 to 28, with higher scores indicating a higher level of FoF. The short FES-I has proved to be a valid measure to assess FoF in frail older adults, including those with cognitive impairment. The standard FES-I cut-off score of ≥11 was used as reference to define elevated levels of FoF.

FoF trajectories for specific patient groups
The course of FoF was modelled for specific subgroups, based on factors expected to distinguish between high or low FoF levels. This led to FoF trajectories for specific subgroups.

First, we compared the course of FoF for patients with prefracture FoF to those without it. Prefracture FoF was assessed in retrospect, related to the period directly before fracture, using a one-item FoF question (‘Are you afraid of falling?’). Prefracture FoF was operationalised as follows: (1) no prefracture FoF (patients reporting ‘not at all’) and (2) prefracture FoF present (patients reporting either ‘a little’, ‘quite a bit’ or ‘very much’).
Second, we explored FoF trajectories for groups based
on FoF status at 6 and 12 weeks. Using the FES-I cut-off score of 11, this led to the following FoF trend groups:
(1) no FoF (FES-I <11 at 6-week and 12-week follow-up); (2) Transient FoF (FES-I ≥11 at 6 weeks and FES-I <11 at 12 weeks); (3) late-onset FoF (FES-I <11 at 6 weeks and ≥11 at 12 weeks); (4) Persistent FoF (FES-I ≥11 at 6 and 12 weeks).

Independent variables
Prefracture mobility and comorbidity have been associated with FoF after hip fracture and were, therefore, included as covariates in the statistical models.22 27 The Parker Mobility Score (PMS) was used as a (retrospective) measure of mobility,29 related to the period directly before fracture. This measurement instrument assesses indoor and outdoor mobility, and the ability to do shopping. Each item is scored as: no difficulty, with walking aid, with assistance or not at all able. The total score ranges from 0 to 9, with higher scores indicating better mobility. For the analyses, prefracture PMS was dichotomised into PMS <9 (assistance needed in mobility) and PMS 9 (independent mobility). The American Society of Anesthesiologists classification (ASA)29 was used to measure general health status (indirectly a measure of medical comorbidity; no other data on comorbidity available in current data set). For the analyses, this variable was dichotomised (category I–II and >II). Age, which has been associated with FoF in older adults, was also included as a covariate.30

Additional variables
For a background description of the study population several characteristics were determined, including age and sex. Independence in activities in daily living (ADL) was measured using the Katz Index of Independence in Activities of Daily Living (Katz-ADL). It was assessed in retrospect, related to the period directly before fracture, to describe prefracture level of functioning.31 Cognitive impairment is common in this population and was determined based on an existing formal diagnosis of dementia, and with the 6-Item Cognitive Impairment Test.32 33 Nutritional problems are frequently reported for this population, and these were measured with the Mini Nutritional Assessment–Short Form.34

To provide insight into the extent of functional recovery after fracture, we used a combined outcome measure, which represents the recovery of independence of ADL.5 12 The combined outcome measure is based on the following variables: (1) mortality; (2) (in)dependent living situation; and (3) recovery of ADL function to prefracture level, measured with KATZ-ADL. Successful recovery was operationalised as: no mortality (all causes) + living independently in a private residence (including a residential home setting and as needed with home care) + recovery to prefracture ADL function (current KATZ ADL ≥ prefracture ADL). Recovery was considered unsuccessful when not all criteria were met. Rates of successful recovery are presented for the 6-week, 12-week and 52-week follow-up for the four FoF trend groups.

Statistical analysis
Descriptive analyses were used to summarise characteristics of the study population. To examine the course of FoF up to 1 year after fracture, we used linear mixed models (LMM). The unconditional growth model—illustrating the course of FoF for the study population as a whole—modelled FES-I as linear function of time; with age, prefracture PMS and ASA classification as covariates (all centred to the mean); in addition to a random intercept. Time was operationalised as weeks since hip fracture.

We examined the effect of prefracture FoF on the course of FoF after fracture, in linear mixed model 1 (LMM1). LMM1 was an extension of our unconditional growth model, which additionally included prefracture FoF as a predictor of the intercept and the slope. In the second linear mixed model (LMM2), we explored the course for the four FoF trend groups. LMM2 included the same covariates as LMM1, with in addition the FoF trend group variable as a predictor of the intercept and the slope. In contrast to the unconditional model and LMM1, the FES-I in LMM2 was modelled from 12 weeks post hip fracture onward, as this model included the independent variable ‘FoF trend groups’, which was based on the observed FES-I at 6 and 12 weeks.

Outcomes are presented as parameter estimates of the linear mixed models. In addition, we present estimated mean FES-I scores at 6, 12 and 52 weeks after fracture for subgroups of our sample. The course of FoF is illustrated in graphs for a patient with sample average values of all covariates. All statistical analyses were performed by using IBM SPSS V.25.0 (Windows), graphs were constructed in R V.4.1.0.

Patient and public involvement
There was no patient and public involvement in any stage of this study.

RESULTS
The study population consisted of all 444 patients with complete data for all variables required for the analyses (figure 1). Most patients were female (n=305; 68.7%) and the average age was 81.9 years (SD: 7.1) (table 1).

Prior to the fracture, a considerable proportion of the population had experienced FoF (n=189; 42.6%). Classification by FoF trend groups shows that absence of FoF is common (no FoF trend group n=190; 42.8%), as is persistent FoF (n=119; 26.8%). Transient FoF accounts for 16.9% (n=75) and late-onset FoF for 13.5% of the population (n=60). Our final study population (n=444) was younger (Δ=−2.5 years [95% CI −3.4 to −1.7]; p<0.001), had a higher prefracture score for the PMS (Δ=1.6 [95% CI 1.4 to 1.9]; p<0.001) and a slightly lower ASA score (Δ=−0.2 [95% CI −0.2 to −0.1]; p<0.001), as compared
with patients that were excluded due to missing data for relevant variables (n=799) (figure 1).

The unconditional growth model demonstrates that the course of FoF up to a year after hip fracture is characterised by a study population-based mean FES-I level that starts just above the cut-off value of 11 at 6 weeks after fracture, and shows a marginal decline over time (figure 2). Estimates are presented in online supplemental appendix 1. One year after fracture, almost one-third of the patients have elevated FES-I levels (n=132; 29.7%). In view of the individual observed trajectories, we see a considerable degree of heterogeneity.

Analyses of FoF trajectories for patients with prefracture FoF (n=189) compared with those without it (n=255), show a decrease in FES-I levels for both groups (figure 3). However, the mean FES-I for the group with prefracture FoF is above the cut-off value of 11 during the entire follow-up, as opposed to the group without prefracture FoF (values presented in online supplemental appendix 2). Although patients with FoF prior to fracture had higher FES-I levels, the effect of prefracture FoF on the course of postfracture FoF was not significant (estimate 0.78; p=0.067).

Figure 4 illustrates the FoF trajectories for each of the four FoF trend groups and shows that each group has a distinct evolution of FoF over time, with different rates of change. The persistent FoF trend group has the highest FES-I levels, and although this decreases to some extent over time, levels remain above the cut-off value of 11 during the entire follow-up (estimated mean FES-I 16.6 at 12 weeks and 14.1 at 52 weeks after fracture). Similarly, the course for the late-onset trend group is characterised by an elevated estimated mean FES-I score, yet levels are lower than in the persistent FoF group and approach the cut-off value of 11 around 52 weeks after fracture. Both the no FoF trend group and transient FoF group have FES-I levels well below the cut-off in the period 12–52 weeks. The heterogeneity in the individual observed trajectories is most profound for the persistent FoF and transient FoF groups (online supplemental appendix 3).

In online supplemental appendix 4, characteristics of each of the FoF trend groups are presented, including baseline characteristics, and data on outcome after fracture. Prior to fracture, both the persistent FoF and late-onset FoF group had more health problems, and reduced mobility function. Twelve weeks after fracture, one-third of patients in the persistent FoF group had a successful recovery regarding independence in ADL function, compared with half of the patients in the transient FoF and late-onset FoF groups, and almost 80 percent in the no FoF group. Insight into the long-term recovery rate is somewhat limited as a result of missing data for a quarter of the population at 1 year after fracture (online supplemental appendix 5). However, the results do point towards better recovery rates for the no FoF group as compared with the other three groups that had FoF at 6 and/or 12 weeks after fracture. We evaluated the proportion of patients with FoF (elevated FES-I levels) 1 year...
Figure 3  Course of fear of falling up to 1 year after hip fracture, for patients with or without prefracture fear of falling. FoF, fear of falling. Falls Efficacy Scale International (7-item) with range 7-28; lower scores indicating less fear of falling. Accentuated solid lines (blue and red) represent the estimated mean FES-I score for the two groups; based on LMM1. The mean FES-I presented in this graph is based on mean-centred values for covariates. It thus represents the course of FoF of a patient with versus without pre-fracture FoF, and sample mean values for all other covariates (e.g. age 81.9 years). The dotted black line represents the FES-I cut-off value of 11. The thin coloured lines represent observed FES-I trajectories of individual patients.

Figure 4  Fear of falling trajectories for predefined ‘fear of falling trend groups’. FoF, fear of falling. Falls Efficacy Scale International (7-item) with range 7-28; lower scores indicating less FoF. Accentuated coloured solid lines represent the estimated mean FES-I score for the different FoF trend groups, based on LMM2. The mean FES-I presented in this graph is based on mean-centred values for covariates. It thus represents the course of FoF of a patient within each of the four FoF trend groups, with sample mean values for all other covariates (e.g. age 81.9 years). The dotted black line represents the FES-I cut-off value of 11. The thin coloured lines represent observed FES-I trajectories of individual patients.

after fracture, based on the estimated FES-I derived from LMM2. FoF was most mostly present in the late-onset FoF (n=26; 43.3%) and the persistent FoF groups (n=101; 84.9%).

DISCUSSION
Main findings
This is the first study to evaluate FoF up to 12 months after hip fracture. The findings illustrate that the population-based mean FES-I is located around the current established cut-off value of 11, and that levels decrease only slightly over time. However, individual patient trajectories are heterogeneous and amidst this diversity, certain subgroups are noteworthy in view of the elevated FES-I levels. Patients with FoF prior to the hip fracture on average had higher FES-I levels during the entire follow-up period, yet this association between prefracture and postfracture FoF was just above the significance threshold. FoF trend groups analyses show that both the persistent FoF group (FES-I elevated at 6 and 12 weeks after fracture) and the late-onset FoF group (FES-I elevated at 12 weeks after fracture), have a long-term course characterised by elevated FES-I levels. The persistent FoF group—accounting for a quarter of the population—has the most profound levels, with mean FES-I remaining well above the cut-off value of 11 up to 1 year after fracture.

Strengths and limitations of the study
An important strength of this study is that, owing to the longitudinal design with 1-year follow-up, it provides novel insight into the long-term course of FoF after hip fracture. The findings contribute to filling an important knowledge gap in hip fracture research. FoF can be considered a potentially modifiable risk factor, that, when addressed adequately, has the potential to improve functional outcome for this vulnerable population. Findings from this study can assist in identifying an appropriate target population for intervention. An additional strength is that the study design is based on a large inception cohort (without inclusion or exclusion criteria), increasing the generalisability of the results to a broad population of patients with hip fracture.

However, some limitations of this current study should be considered. First, the analyses were based on a subpopulation—patients with complete cases of FES-I scores at 6 and 12 weeks. This reflects a population that survived the first 3 months after fracture, was able to visit the outpatient clinic and did not have severe cognitive deficits that could interfere with the assessment of the FES-I. Patients with advanced cognitive problems or serious physical and functional impairment (ie, residing in nursing home) may be underrepresented in this population. Indeed, we found significant differences between the selected and excluded population regarding the covariates in our model—age, ASA classification, PMS. However, for age and ASA the differences may be considered modest, and we can question the clinical relevance. Second, prefracture FoF was...
assessed in retrospect, which in theory could lead to recall bias. This was also assessed using a one-item FoF question, which complicated the comparison between prefracture and postfracture FoF. Future studies should preferably use FES-I for all assessments, in order to enable comparison of the extent of FoF before and after fracture, and hence improve insight into the course of FoF, with the fracture as an intermediate event. Finally, we did not assess mood and anxiety in this study. In community-dwelling older adults depression has been associated with FoF (and activity restriction). In recent FoF literature, it has also been suggested that anxiety determines whether FoF becomes maladaptive. Neuroticism has also been identified as a risk factor for high FoF after fracture. We recommend that future studies evaluate these psychological factors in relation to the course of FoF.

**Comparison with current literature on FoF**
We can question whether FoF, in patients with hip fracture, may to some extent be a normal or adaptive response to the recent fall-related medical event and current physical impairment. Oshima et al found that for community-dwelling older adults, mobility problems (standing balance and gait) were associated with the development of FoF. This concept may also be applicable for the early stage after fracture, which is characterised by sudden impairment of gait function. This could partly explain our finding that, shortly after hip fracture, the mean FES-I is located around the cut-off value. Another important finding in literature is that the negative effects of FoF on functional recovery are not found for FoF in the very early phase after hip fracture, but only from 6 weeks after fracture and beyond. How this finding relates to the natural course of FoF after fracture is still unknown, owing to a research gap on this subject. Longitudinal data on FoF after hip fracture is scarce and current literature focuses mainly on the cross-sectional presence of FoF. Only two longitudinal studies provide some insight into FES-I levels over time. Similar to our findings, the population-based mean FES-I levels in these studies were ≥11 in the early stage after hip fracture. Furthermore, in these studies, FoF levels were found around the FES-I cut-off score, at 12 weeks after fracture, and 6 months after rehabilitation, respectively. This supports the overall course of FoF observed in our study.

However, as our findings demonstrate a considerable degree of heterogeneity in the individual trajectories, it seems helpful to explore specific subgroups, in order to identify patients with (1) excessive FoF or (2) persistent FoF. Both features could be indicative of maladaptive FoF in this population, that is, FoF that impedes physical activity and daily functioning. To examine whether FoF at 12 weeks is related to an increased risk of FoF in the long term (1 year after fracture), we explored FoF trajectories from 12 weeks onward, for the four different trend groups, based on observed FoF at 6 and 12 weeks. Only one previous study evaluated specific FoF trajectories, but within an earlier timeframe, that is, in the period 4–12 weeks after fracture. Using latent class analysis to model the course, the study found three distinct FoF trajectories, namely minimal FoF (72%), decreasing FoF (17%) and increasing FoF (11%). Despite differences in timeframe and methodology, some parallels can be drawn between study findings. First, a considerable part of the population either has low FES-I levels, or moderate FoF levels around the FES-I cut-off of 11. Second, there is a small group with elevated FES-I levels in the early stage after fracture (4–6 weeks) who demonstrate a trend of recovery in the subsequent period (decreasing FoF group, respectively, transient FoF trend group in our study). Third, patients with a trajectory characterised by repeated elevated FES-I levels up to 12 weeks, have substantial levels at onset (4–6 weeks after fracture), with a mean FES-I around 16. An important finding with regard to this last mentioned group—the persistent FoF group—is that patients in this group have the poorest recovery of independence in ADL function, with only one-third of the patients showing successful recovery at 12 weeks after fracture. The other group with FoF at 12 weeks, the late-onset FoF group, also had a recovery rate that was somewhat limited. This extends on previous literature showing that high levels of FoF at 12 weeks after fracture are related to poor long-term recovery.

This study also examined prefracture FoF in relation to the FoF after fracture, as it is undetermined whether prefracture and postfracture FoF can be considered a continuum. At present, there is no comparative literature on this topic, although one previous study provides evidence that prefracture FoF affects short-term functional recovery. Our findings illustrate that, contrary to those without prefracture FoF, patients with prefracture FoF have sustained elevated FES-I levels over time. The mean FES-I score for the group with prefracture FoF is approximately 2 points higher compared with the group without prefracture FoF. Interpretation of this between-group difference is complicated by the fact that a clearly defined minimal clinical important difference for FES-I score is absent. However, a previous intervention study on FoF referred to a difference of 2 points on the 7-item FES-I as a possible favourable outcome. Thus although the association was not statistically significant, the observed difference between groups with and without prefracture FoF indicates that prefracture FoF may to some extent influence FoF after fracture, and that it may be relevant to assess this in clinical practice.

**Implication for clinical practice**
When FoF is evident and impairs daily functioning, existing treatment approaches for community-dwelling older adults are recommended. Functional recovery of lower extremity function after hip fracture can continue to almost a year after fracture, and we, therefore, expect that treatment for FoF in advanced stages after hip fracture has potential to optimise functional ability. Considering the high FES-I levels, the chronic nature of the FoF and the poor recovery of independence in ADL function
in the persistent FoF trend group, we believe that it is mainly this group—roughly a quarter of the population—that is at risk for maladaptive FoF and could consequently benefit from intervention. Timely identification of these patients requires a structural approach to assessing FoF up to at least 12 weeks after fracture. This may call for efforts from various healthcare professionals in the different care settings that the patient passes through in the rehabilitation process. Essentially, we recommend screening for prefracture FoF immediately after fracture to limit risk of recall bias, to assess the FoF levels in the acute phase, at onset of rehabilitation and at 12 weeks after fracture.

CONCLUSION

Although FES-I levels decrease to some extent in the year following hip fracture, FoF as defined by a FES-I score ≥11 remains present over time for a considerable part of the population. Patients with persistent FoF at 12 weeks have the highest FES-I levels during the entire follow-up, a high rate of FoF 1 year after fracture, and limited recovery of independence in ADL function. These patients may benefit from an intervention to address the FoF. To identify patients at risk for high or persistent FoF in a timely manner, we, therefore, recommend structural assessment of FoF, including screening for (prefracture) FoF directly after fracture, at onset of rehabilitation, and 12 weeks after fracture.

Acknowledgements

We are very grateful to the ‘Hip Fracture Centre’ of the Haaglanden Medical Centre for allowing us to use this current dataset. We thank all the staff members of the interdisciplinary Hip Fracture Centre for their contribution to the data collection.

Contributors

MvDS and AHPN designed the current data collection structure for this inception cohort and monitored the data collection. MvDS performed the data analysis, together with MLH and MeV. MNS-B, MLH, WPA, JCMvH and MeV were involved in the interpretation of the results. MNS-B drafted the manuscript. All authors contributed to the manuscript, provided feedback, and have read and approved the final version. The corresponding author (MNS) is the guarantor of this manuscript.

Funding

This study is based on the database of the ‘Hip Fracture Centre’ of the Haaglanden Medical Centre. The development and organisation this database, with ongoing data collection, is funded by the Department of Surgery of the Haaglanden Medical Centre. The current study received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors. ZonMW and the Leiden University Medical Center (training centre for Elderly Care Medicine) support this study.

Competing interests

None declared.

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication

Not applicable.

Ethics approval

This study involves human participants and was approved by METC Southwest Holland; protocol number 16-059. Because of its observational design, informed consent was not required according to the Dutch regulations.

Provenance and peer review

Not commissioned; externally peer reviewed.

Data availability statement

Data are available on reasonable request.

Supplemental material

This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

Open access

This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/.

ORCID iDs

Maaike N Scheffers-Barnhoorn http://orcid.org/0000-0002-9580-0208
Wilco P Achterberg http://orcid.org/0000-0001-9227-7135

REFERENCES


