PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf**) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Finnish Trial on Practices of Anterior Cervical Decompression and Fusion (FACADE): A Protocol for a prospective randomised non-inferiority trial comparing Outpatient vs. Inpatient care
AUTHORS	Lönnrot, Kimmo; Taimela, Simo; Toivonen, Pirjo; Aronen, Pasi; Koski-Palken, Anniina; Frantzen, Janek; Leinonen, Ville; Silvasti-Lundell, Marja; Förster, Johannes; Jarvinen, Teppo

VERSION 1 – REVIEW

REVIEWER	Masao Koda Department of Orthopedic Surgery, University of Tsukuba, Ibaraki, Japan
REVIEW RETURNED	14-Aug-2019

GENERAL COMMENTS	The authors described the study protocol of prospective randomized non-inferiority trial comparing outpatient vs inpatient care for ACDF. The study design is reasonable and comprehensive to elucidate the effectiveness of outpatient care for ACDF. However, I have one concern about complication. Although I can understand that there is no significant difference in complication rate between outpatient and inpatient groups, is there any difference in outcome of complication (e.g. dysphagia, hematoma, etc.)

REVIEWER	Carmen Vleggeert-Lankamp Leiden University Medical Centre, Leiden, the Netherlands Covidien sponsors a trial on legpumps in neurosurgical surgery. Ynske Meyes Fund and SAG fund sponsor a trial on epidural injections in sciatica. These are all investigator initiated trials. The payment is not made to my own account but to our research department. Board of CSRS Europe and Netherlands Neurosurgical Society (NVvN), faculty for EANS, CSRS, Eurospine and webinar for AO spine.
REVIEW RETURNED	20-Aug-2019

GENERAL COMMENTS	The goal of this research project is clear and the outcome is important. However, it is to be expected that the problem of sending patients home on the day of surgery can be that they are insecure of the follow up trajectory. The authors mention in the abstract that the main purpose is to emphasize the perception of symptom relief and ability to return to normal work. however, the primary outcome measure focuses on the relief of arm and neck pain. That is not the primary outcome measure to be interested in. I sure do believe that the surgeons can operate properly and give satisfactorily results. A primary outcome parameter focusing on patient perception of care and return to work should be chosen in my opinion.

	Furthermore: the set up is not adequate. The patients in the group that is sent home at the same day is called weekly by a research nurse. This in itself is comforting and prevents them to contact other caretakers. Thus: the outcome of the study will not be representative for daily clinical practice. Another important outcome measure is the scoring of the times and intensity of the care that the patients seeks after surgery. It is to be expected that the patient that is being sent home too early will call the family doctor or the nurses or the secretaries with complaints. This is very time consuming and it should be scored in the study. In conclusion: the idea of the study is good, but the set up of the study needs improvement in order to deliver conclusions that are relevant for daily clinical practice.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: Masao Koda
Institution and Country: Department of Orthopedic Surgery,
University of Tsukuba, Ibaraki, Japan

The authors described the study protocol of prospective randomized non-inferiority trial comparing outpatient vs inpatient care for ACDF. The study design is reasonable and comprehensive to elucidate the effectiveness of outpatient care for ACDF. However, I have one concern about complication. Although I can understand that there is no significant difference in complication rate between outpatient and inpatient groups, is there any difference in outcome of complication (e.g. dysphagia, hematoma, etc.)

Authors' response: We thank the reviewer for the careful review of our paper. We share the reviewer's view on the importance of recording (and reporting) complications in detail. Accordingly, in the submitted manuscript, we did have "complications" as our secondary outcome, and thus, as shown in table 2 (the timetable for assessment of adverse effects), we are committed to recording and assessing all complications directly related to the study interventions. The complications to be recorded at each follow-up assessment time point include postoperative dysphonia, odynophagia, hematoma, as well as all other potential complications. Furthermore, the participants will also be encouraged to contact the hospital if any adverse effects occur. We expect that by this prudent follow-up scheme/protocol, we should be able to detect and report, if there will be any between-group differences in the complications.
Authors' action: As noted, complications are collected (and will be reported) in detail. No action.

Reviewer: 2
Reviewer Name: Carmen Vleggeert-Lankamp
Institution and Country: Leiden University Medical Centre, Leiden, the Netherlands

The goal of this research project is clear and the outcome is important.

Authors' response: Thank you for the careful review of our paper and encouraging overall comments on our trial.

However, it is to be expected that the problem of sending patients home on the day of surgery can be that they are insecure of the follow up trajectory.
Authors' response: We thank the reviewer for this attentive remark. Although we agree with the reviewer that sending patients home on the day of surgery can make them insecure of the follow-up trajectory, we respectfully remind that this question is actually one of the main objectives (hypothesis) of the trial, i.e., to study whether there is a difference in the patients' perception between those discharged on the day of surgery and those kept overnight. However, it is also recalled here that we will make every effort to ascertain that the follow-up of both groups is as identical as possible.

Authors' action: Prompted by reviewer's remarks we have rephrased the chapter "informed consent" as follows:. We will ensure that patients understand that the surgical procedure they undergo as well as follow-up protocol will be identical irrespective of study group allocation, and that the randomisation only occurs after the surgery.

The authors mention in the abstract that the main purpose is to emphasize the perception of symptom relief and ability to return to normal work. However, the primary outcome measure focuses on the relief of arm and neck pain. That is not the primary outcome measure to be interested in. I sure do believe that the surgeons can operate properly and give satisfactorily results. A primary outcome parameter focusing on patient perception of care and return to work should be chosen in my opinion.
Authors' response: We thank the reviewer for pointing out this particularly important issue, the appropriateness of our primary outcome. We understand the reviewer's notion that patients' perception of care and return to work should be chosen as the primary outcome(s) over relief of arm and neck pain. In fact, we have devoted a considerable amount of time and consideration into contemplating as to what represents the most appropriate primary outcome. Given that after our careful consideration, we have chosen relief of arm and neck pain as the outcomes of interest (rather than return to normal work, as suggested by the reviewer), a few words about our rationale seem warranted here. Although we understand the contention that return to work indicates that a person has reached a stable health status in his/her recovery, this may not be entirely true/accurate, as a relatively high percentage of patients who initially return to work later fail to make this status sustainable. Given that we expose the patients in this trial to a relatively major surgery, we felt that our primary outcome should reflect a health status as stable as possible (rather than a transient state). Also, the hallmark symptoms of this disease – and also the reason the patients seek for help/medical attention – is neck pain radiating to the arm, we felt that also from this perspective, the Neck Disability Index (NDI) would be the most appropriate primary outcome. In the end, we find it highly likely that alleviation/persistence of neck pain is also closely correlated/associated with functional recovery (return to work), and accordingly, is a more valid measure of the overall treatment success.

Authors' action: Prompted by this very attentive remark by the reviewer, we decided to add discussion that hopefully better explains our rationale for choosing NDI – instead of return to normal daily activities and/or return to work – as our primary outcome. The added section (page 19) is as follows: "In this FACADE trial, we primarily set out to determine whether the outcome of outpatient group is non-inferior to current standards of care (overnight stay) at 6 months postoperatively. Given that the hallmark symptom of this disease – and also the primary reason the patients seek for medical attention – is the disability caused by radiating arm pain, we felt that the Neck Disability Index is the most appropriate primary outcome for our trial. Although one can argue that rapid return to normal daily activities and work would be a better indication that a person has reached a stable health status, such contention may not be entirely accurate. Comprehensive data on sustainable return to work (RTW) shows that a variety of personal and social factors have positive and negative influences on

sustainable RTW (28). Obviously, the social environment and how it interrelates with personal factors like attitudes towards work and self-efficacy play a role alongside the alleviation of neck pain as predictors of RTW."

Furthermore: the set up is not adequate. The patients in the group that is sent home at the same day is called weekly by a research nurse. This in itself is comforting and prevents them to contact other caretakers. Thus: the outcome of the study will not be representative for daily clinical practice.
Authors' response: We thank the reviewer for these valuable comments, which made us realize that this section was not sufficiently unambiguous in the former version. In essence, patients in both groups (those sent home at the same day and those staying in the hospital overnight) are contacted weekly, so although it may not exactly represent daily clinical practice everywhere in the world, there is no between-group difference in this respect, and accordingly, our comparisons are not biased.
Authors' action: No action.

Another important outcome measure is the scoring of the times and intensity of the care that the patients seeks after surgery. It is to be expected that the patient that is being sent home too early will call the family doctor or the nurses or the secretaries with complaints. This is very time consuming and it should be scored in the study.
Authors' response: Thank you for expressing an interesting hypothesis on how patients might behave and what downstream effects their behavior might have on health care utilization. We probably both agree that until this hypothesis is tested, it remains a hypothesis, only. However, the reviewer's attentive remark made us realize that our description of the follow-up scheme was not unambiguous enough, as we do plan to inquire and collect the healthcare utilization at each follow-up time point. In essence, each time a patient is contacted (either by phone or via our electronic system), we ask them to report any contacts to the healthcare providers.
Authors' action: We have rephrased the follow-up chapter as follows (page 13): "We collect data on healthcare resource utilization at the 1-, 3-, and 6-month follow-ups. In addition, we also encourage the patients to contact the FACADE study nurse if they encounter any problems that require medical attention at any time over the course of the follow-up."
In conclusion: the idea of the study is good, but the set up of the study needs improvement in order to deliver conclusions that are relevant for daily clinical practice.
Authors' response: Thank you very much for these highly attentive and constructive comment. We feel that this feedback has truly improved our paper.

VERSION 2 – REVIEW

REVIEWER	Masao Koda Department of Orthopedic Surgery, Tsukuba University, Ibaraki, Japan
REVIEW RETURNED	01-Oct-2019

GENERAL COMMENTS	The reviewer agreed with the author's response. Now, the reviewer think that the present manuscript is acceptable for publication.