Author’s response to reviews

Title: Customized Registry Tool for Tracking Adherence to Clinical Guidelines for Head and Neck Cancers: Protocol for a Pilot Study

Authors:
Matthew Hickey (matt.hickey@ucsf.edu)
Sarah Lisker (sarah.lisker@ucsf.edu)
Shauna Brodie (shauna.brodie@ucsf.edu)
Eric Vittinghoff (eric.vittinghoff@ucsf.edu)
Marika Russell (marika.russell@ucsf.edu)
Urmimala Sarkar (urmimala.sarkar@ucsf.edu)

Version: 3 Date: 11 Dec 2019

Author’s response to reviews:

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

BERKELEY * DAVIS * IRVINE * LOS ANGELES * RIVERSIDE * SAN DIEGO * SAN FRANCISCO * MERCED

SANTA BARBARA * SANTA CRUZ

DEPARTMENT OF MEDICINE
DIVISION OF GENERAL INTERNAL MEDICINE
ZUCKERBERG SAN FRANCISCO GENERAL
CENTER FOR VULNERABLE POPULATIONS UCSF Box 1364
San Francisco, CA 94143-1364
Tel: (415) 206-4273, Pager (415) 443-8841
Dear Dr. Gopalan and the Editorial Board at Pilot and Feasibility Studies,

Thank you for giving us the opportunity to submit a second revision of our manuscript (PAFS-D-19-00114R2) entitled “Customized Registry Tool for Tracking Adherence to Clinical Guidelines for Head and Neck Cancer: Protocol for a Pilot Study” for consideration as a study protocol in Pilot and Feasibility Studies.

We are pleased to address the editorial comments below. We have revised our manuscript by incorporating your recommendations throughout. Included in our revision is a clean version of the revised manuscript along with a track changes version of the revised manuscript. Reviewer comments are reproduced in bold with our response following and updated text in italics. We have indicated precisely where in the clean version of the revised manuscript we have addressed reviewer comments and suggestions.

All authors have read and approved submission of the manuscript. Authors claim no conflicts of interest. The manuscript has not been published and is not being considered for publication elsewhere.

Thank you for considering our manuscript for publication in Pilot and Feasibility Studies.

Sincerely yours,

(electronically submitted on behalf of all authors)

Corresponding Author

Urmimala Sarkar, MD, MPH
Professor, University of California San Francisco
Zuckerberg San Francisco General Hospital, 1001 Potrero Ave, Building 10, Ward 13
San Francisco, CA 94143
Urmimala.sarkar@ucsf.edu
628-206-4273

Editor's comments:
1) There are no clearly stated feasibility objectives for the study. These need to be provided with clear feasibility outcomes and criteria for determining success to proceed to main trial.

We have added the feasibility outcomes and the criteria for moving to the larger trial (lines 222-232):

The key implementation outcome is feasibility. We will also measure several components of tool utilization to better understand the actor, dose, temporality, and action target of the intervention.(16) Data collection on these parameters will occur through a quarterly survey of clinic staff using the tool and through five randomly selected clinic days when the investigators will observe clinic staff and any
use of the tool that occurs. The survey will ask staff to report their role in the clinic and recall for the prior week the amount of time that the tool was used, timing of use, and number of patients outreached through use of the tool. The feasibility objective for this pilot study is to achieve consistent use throughout all clinic sessions reaching all eligible patients. The feasibility outcome which will determine success and trigger proceeding to the main trial is achievement of significant use: use during at least 80% of clinic sessions and for 80% of eligible patients.

2) The sample size seems to be based on significance testing for effects -- which is inconsistent with feasibility evaluation as the primary focus. Thus, this study is designed as a definitive trial rather than a pilot trial intended to provide information to be used in the design of the main trial. Estimation of preliminary effects should be considered secondary objectives, and such estimates should be provided as point estimates (95% CIs) without tests of significance.

We agree with the editor that clarification of the minimum detectable effects was needed. We have added to the text that the efficacy outcomes are secondary objectives. With this sample size, we have limited power and can only detect rather large effects. We have stated that explicitly in the text. We would prefer to keep the tests of significance in the simulation; otherwise the simulated effects are difficult to interpret. Though feasibility is the primary outcome that will determine progression to a full-scale trial, preliminary effect estimates will also guide this process. For example, if preliminary effect estimates approach 1.0, it will prompt further investigation as to the reasons why the tool might not be improving time to diagnosis and treatment, and may lead to modification of either the tool or the implementation process prior to a full-scale trial. We revised substantially (lines 243-255):
Estimation of preliminary effects should be considered secondary objectives. The sample size we propose is based on feasibility outcomes, and therefore the simulations below demonstrate that the pilot sample size would only detect a substantial effect size. Depending on the feasibility outcomes, we would proceed to a larger trials with the ability to detect more modest effects. With the present number of patients, in Cox models for time to event, the sample of 300 will provide 80% power with in two-sided tests with alpha of 0.05 to detect a hazard ratio of 2.25 for the effect of the intervention, after adjusting for a linear temporal trend as well as confounders. For binary outcomes including loss to follow-up and completion of stages, it will provide 80% power to detect intervention odds-ratios of 3.4 to 6.7, depending on the number of patients included in the analysis (200-300) and the prevalence of the outcome (20 to 50%), again after adjusting for a linear temporal trend and confounders. These estimates were obtained using simulations implemented in R Version 3.4.3.