PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Evaluation of Gold Coast Integrated Care for patients with chronic disease or high-risk of hospitalisation through a non-randomised controlled clinical trial: a pilot study protocol.
AUTHORS	Scuffham, Paul; Mihala, Gabor; Ward, Lauren; McMurray, Anne; Connor, Martin

VERSION 1 - REVIEW

REVIEWER	Laurent Billot The George Institute for Global Health, Australia
REVIEW RETURNED	27-Mar-2017

GENERAL COMMENTS	This article presents the protocol for the evaluation of Gold Coast Integrated Care using a propensity-matched control group. Overall, the article is clear but I do have a few questions and comments listed below. 1. Abstract, methods and analysis, last paragraph: 1.1. consider replacing "will use a range of advanced statistical techniques" with a more informative description of outcomes (e.g. service utilisation and costs). 2. Strengths and limitations of this study: 2.1. consider discussing potential biases due to lack of randomisation and potential counfounders. 2.2. consider discussing potential issues related to regression to the mean effects as seen in previous trials (e.g. integrated care pilots in the UK and CDMP evaluation in Australia) 3. Introduction: 3.1. In addition to the political and private/public fragmentation of the health system, the authors should mention the fragmentation in the continuum of care in particular between general practice and acute care. 3.2. Consider adding references to recent Australian initiatives e.g. NSW Health CDMP evaluation (http://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1002035) 4. Participants and recruitment: 4.1. Please clarify how the 15 control practices will be selected and whether they will be matched to the 15 intervention practices. In addition, please comment on the risk of biases due to potential systematic differences between practices. 4.2. The authors mention six processes to identify high risk patients into the intervention group; however, the overarching eligibility criteria is unclear and should be made more explicit. Is the criteria

	as follows “1) patients who in the past 12 months had ≥ 1 inpatient admissions in the past 3 years AND 2) ≥ 1 emergency department presentations in the past 3 years AND 3) ≥ 5 current medications AND 4) ≥ 20 general practice visits AND 5) have a coded diagnosis of diabetes, chronic heart disease, chronic obstructive pulmonary disease, or chronic kidney disease”? In addition, to avoid systematic differences between the intervention and control patients, the eligibility criteria should be as similar as possible between the two groups and assessed on the same type of data. They currently look different. 4.3. Please expand of the type of demographic and chronic health characteristics that will be considered for propensity matching. 4.4. “The control group will receive usual care”. The use of future tense is confusing given that the 1,500 intervention patients appear to have already been recruited. Please clarify whether the control individuals have already been identified. 4.5. Please provide details of authority responsible for linking and de-identifying individual information 5. Power, detectable difference and sample size 5.1. Please comment on the “clinical” relevance of the detectable differences mentioned for each outcome. 5.2. Please note that there are methods that can provide power calculations in case of unequal cluster sizes and different number of clusters per arm e.g. http://bmcmedresmethodol.biomedcentral.com/articles/10.1186/1471-2288-6-17 6. Quantitative analyses 6.1. Please clarify whether the choice of analysis based on the distribution of data will be done in a blinded manner i.e. prior to seeing any result by arm (intervention vs control) 6.2. Given the complexity of the analyses and the number of outcomes, please clarify your plan to write a separate analysis plan, the expected timing and, if relevant, dissemination.

REVIEWER	Aaron Spaulding Mayo Clinic, USA
REVIEW RETURNED	24-Apr-2017

GENERAL COMMENTS	This is an interesting, and needed study, and the authors have provided good insight into their study methods. They are attempting to determine if integrated care will help improve the health of chronic disease patients. Overall, the protocol is well written and provides the context, procedures and outcomes of interest for the study. There are a few areas which need additional clarification as outlined below. First, within your study design you indicate your primary question as "Did GCIC reduce overall costs of delivering health care services to the GCHHS and improve health outcomes for high risk patients with complex needs?" As stated, this question would only be answered with a pre- post- design to define how outcomes for these patients changed after the intervention was implemented. The protocol which follows seems to better answer if the GCIC experiences reduce costs compared to standard care procedures. As the authors indicate, this study is likely to suffer from selection

	bias on multiple different levels. The ability for practices and thereby patients to opt into the intervention arm creates the opportunity for different groups to be employed in each arm. Therefore the need to match patients between the control and intervention arm is required. The authors indicate they will indeed do so, but provide little information on the characteristics they will match patients on. Page 5 line 8-10 provides indication that a range of demographic and chronic health characteristics will be used. Please provide greater detail on the characteristics that will be used. Also, some indication of the current patient populations available at each participation location will provide greater context as to the likelihood that the number of similarly characterized patients will be available. In addition, the selection and matching of the control arm sites isn't well explained. Please describe how the additional 15 sites will be chosen and how they will relate to the initial 15 sites which opted in. Similarly, it appears that the inclusion criteria for the intervention arm are high risk patients, but it is not clear high risk patients are also the group that is being recruited from the control arm sites. In Table 1, a passive control group arm is mentioned, however this isn't indicated in the text, or at least not clearly. Please more clearly define this group as well as your purpose in using the group passively. In addition, one of the inclusion criteria for the intervention arm includes "purposely designed risk of hospitalization scores" p 4 line 34. Please describe what this means and what hospitalization scores will be used in both groups. Within the Qualitative Analysis section (Page 9), please describe the number of focus groups for each time period as well as the number of participants. A table here would be helpful. Statistically, I have some concerns that you will find enough variance in some of your outcome measures, and your sample size may be too small to determine differences in all of the outcomes listed for this study. Please report the Validity and Reliability scores for the patient questionnaires which will be using (AQOL-4d, ICECAP-O-5, LSNS-6, etc). In terms of the participant enrollment, interventions, etc a figure would be helpful. In terms of data monitoring, it isn't clear which of the committees listed on page 3 will be responsible for data monitoring. In addition the description of interim analysis and stopping guidelines could be more complete. Finally, the plans for communicating important protocols to groups other than the IRB needs further development. Thank you for the opportunity to review your protocol. I hope these comments serve to strengthen your important work.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1

Responses:

1. Abstract, methods and analysis, last paragraph:

1.1. Thank you for this suggestion. Outcomes have been listed in this paragraph.

2. Strengths and limitations of this study:
2.1 & 2.2 Selection bias due to lack of randomisation has been included. Other potential confounders have also been added to strengthen this section. We believe regression to the mean is better discussed in reports and publications after the completion of the trial, and not in the protocol paper. It is an issue that is routinely dealt with during statistical analyses.

3. Introduction:
3.1 Thank you, fragmentation between general practice and acute care has been included in this section. Reference added.

4. Participants and recruitment:
4.1 The selection methods for the control practices have been added, with risks for potential differences between practices included in this section and in 'Strengths and Limitations'.
4.2 Eligibility for the program has been reworded – we trust that this clarifies that patients identified as high risk of hospitalisation are eligible for the program.
4.3 Matching method now explained in more detail in the Participants and recruitment section
4.4 Control participants have been identified - the tense has been corrected.
4.5 Public Health Act approval has been received for the matching exercise – this has been detailed here.

5. Power, detectable difference and sample size
5.1 The study is an economic and health services study rather than a clinical study. Therefore, the clinical relevance of differences in costs / hospitalisations is not relevant here.
5.2 We thank the reviewer for the suggestion. The relevant part in the Power, detectable difference and sample size section was reworded. These calculations were completed a priori, expecting reasonably balanced cluster sizes.

6. Quantitative analyses
6.1 Blinding the statistician to group allocation has the potential to reduce bias, however it is practically impossible in this case (given the greatly differing group sizes)
6.2 No separate analysis plan is being prepared as this is not a RCT, but a health services study. The primary analyses are described in this protocol.

Reviewer 2
Responses:

1.Thank you for this recommendation. We realise this is a compound question. As such we have re-written this question as two co-primary questions (one around reducing costs, and another around improving health outcomes) and made it explicit these questions are compared with usual care. That is, a pre-post intervention group and a pre-post usual care group. The usual care group is necessary given the anticipated attrition rates due to deaths in this high risk population with complex conditions.

2. Thank you for this suggestion. The participant matching criteria has been clarified, and a description of how the control practices were identified and recruited has been added to this section.

3. Thank you for this feedback – eligibility criteria for both intervention and controls has been reworded. The purpose of the passive control group has also been mentioned. The risk of hospitalisation score has now described in greater detail. As this score is reliant on GP data, this score has not been used for the control group.

4. Thank you for this suggestion – additional focus group detail has been included.

5. Thank you for the point raised. The reviewer appears to be concerned about outcome variables with too much variance, where the results would not be able to provide strong evidence to reject the null hypothesis of no difference between groups, given the sample size. These concerns are best answered by properly conducted sample size determination, where the effect sizes are specified as clinically/economically significant values.

6. Validity and reliability scores have been included as a footnote after table.

7. Thank you for this suggestion. A graph has been included in the manuscript.

8. Evaluation data is monitored by the GCIC Evaluation Steering Committee which is now mentioned in the text. Dissemination to other groups has also been described further.

I thank you again for reviewing our manuscript and providing the opportunity to resubmit with revisions. We look forward to hearing the outcome of our revised protocol shortly.

VERSION 2 – REVIEW

REVIEWER	Laurent Billot The George Institute for Global Health, Sydney, Australia
REVIEW RETURNED	23-May-2017

GENERAL COMMENTS	The authors have adequately addressed most of my comments. I now find the paper much easier to understand in particular around the creation of the control group. My only remaining concerns relate to: a) The statement that deciding the best model will not be done in a blinded manner b) That no separate analysis plan will be developed on the basis that is is not a randomised clinical trial. I believe that the fact that this is not a RCT does not preclude from preparing an analysis plan. In fact, given some of the analytical complexities and the risk of biases inherent to non-randomised studies, one might argue that an analysis plan is as least as important. It would not need to be as extensive as one prepared for a RCT but provide enough details about the choice of models, the process for adjusting for confounders, handling of missing data, sensitivity analyses etc. I also think that the fact that this is not a randomised study should not prevent someone from making model choices based on the overall data distribution (i.e. before performing analyses broken down by treatment arm). Although these two issues do not impact on the current protocol paper, I would encourage the authors to consider a separate analysis plan and a process by which the final models can be selected without being influenced by the effect of the intervention.