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)	Health outcomes of patients with chronic disease managed with a healthcare kiosk in primary care: protocol for a pilot randomised controlled trial
AUTHORS	Ng, Grace; Tan, Sze Wee; Tan, Ngiap Chuan

VERSION 1 – REVIEW

REVIEWER	Dr. Iñaki Martin Lesende Bilbao-Basurto Integrated Healthcare Organization (IHO), San Ignacio General Practice, Basque Health Service - Osakidetza, Bizkaia, Spain
REVIEW RETURNED	31-Oct-2017

GENERAL COMMENTS	This is a well-structured and interesting study as it will develop and evaluate an intervention using a practical ICT to cope with the increase of the elderly population and chronic diseases particularly in primary care. My main suggestions for the manuscript can be found below. In the ABSTRACT some aspects should be improved or better explained: The patients included are not properly defined in this important section of the document. Only two primary outcome variables/measures are indicated, blood pressure (BP) and haemoglobin A1c (HbA1c) levels, as they were the most important outcome variables; however, there are non-diabetic patients where the control and results are not assessed through the HbA1c. This, as I will explain later, is a general drawback when explaining the outcome variables in the study. In keywords, "healthcare kiosk" is not a mesh term; it could be changed by a mesh term?. The STUDY AIM would be more understandable if it was presented in positive wording (instead of "... show non-inferiority ..."). And, included in the aim, the same considerations I made related to the main outcome measures, BP and HbA1c. METHODS The setting should be better explained in this study (social and demographic characteristics, urban / rural setting, health suport and network ...). Since only one health center is being evaluated, these characteristics are important to assessing its transferability and external validity.

	In the study, patients over 75 years are excluded though they represent a very important proportion of patients with chronic diseases. The reasons for this decision could be explained. The main outcome variables could be reconsidered or better explained. BP and HbA1C are indicated as the main ones. However, the clinical attitude and control are subsequently based on risk stratification and different variables depending on whether or not they are diabetic patients; for example, LDL levels are important in the latter. It might be more convenient to evaluate the degree of control (well, sub-optimally, and poorly - controlled) as the main outcome variable?. A stratified sample could also have been applied according to being diabetic or not in order to better consider and assess the outcome variables. This would also modify the estimated sample size. FIGURE 3 is partially unfocused, it could be improved. The pathologies indicated in TABLE 1 and those indicated in the text in the inclusion do not coincide. Considering a level of HbA1c <7 as good control might be very rigid for diabetic patients with certain characteristics (comorbidity or duration of the disease, according to recent clinical practice guidelines). It is indicated that HbA1c is measured in a diabetic patient with a capillary blood sample. How is it measured for those patients who use the healthcare kiosk? Some assessment should be made referring to specific costs, including the cost of the technology (healthcare kiosk and its maintenance). Best regards and good luck.

REVIEWER	Chris Salisbury University of Bristol, UK
REVIEW RETURNED	04-Dec-2017

GENERAL COMMENTS	Thank you for asking me to review this trial protocol. I have tried to highlight issues which may need more clarification or justification in the protocol and other things which it may not be too late to change. When mentioning page numbers this relates to the numbers at the top of the combined PDF from BMJ Open. I recommend the authors consider a more sophisticated approach to analysis using linear and logistic regression for continuous and categorical variables respectively, taking into account any variables which are unbalanced at baseline. The authors may wish to explain more about their choice of inclusion criteria in relation to their choice of outcome measures. For example, they are including people with hyperlipidemia and coronary heart disease who are not hypertensive or diabetic at baseline. I cannot see how HBA1C can be used as a primary outcome measure for people who are not diabetic but perhaps that's not the intention. Perhaps the applicants only intend to use HBA1C as an outcome measure in those who are diabetic. Although BP is a relevant

	outcome for all of the diseases which form the inclusion criteria it would be surprising if it changes much in people who are well controlled at outset and in whom hypertension was not their problem. Perhaps the applicants could explain how they will combine BP and HPA1C in a population not all of whom are diabetic or hypertensive. It would be helpful if they could explain somewhere in the protocol when in the process patients have their blood taken, given that the results of these tests feed into the decision about whether or not they can collect their medication. Do they have the blood taken and analysed just before the kiosk visit? The applicants say that the accuracy of the kiosk measurements will be verified (p12, line 19). Could they explain how they will do this verification? The applicants state on p11, line 20 that people who have suboptimal or poorly controlled disease will be taken out of the study and attend routine clinic consultations for their subsequent follow up visits and yet on p14, line 37 they say the study will be analysed by intention to treat. If they take patients out of the study who have poorly controlled disease then by definition the only people remaining in the study at the end will be those with well controlled disease and equivalence between the study arms is guaranteed. It may be appropriate that people with suboptimal control are taken out of kiosk care and followed up through clinic consultation, but following the intention to treat principle its very important that they stay in the analysis. Keeping people with poor control in the analysis to the end applies to both arms of the trial. This seems a very small study but the reason for this becomes clear when one looks at the power calculation. The authors have assumed a standard deviation in BP of 9.6 and a non-inferiority margin of 10, i.e. an effect size of more than 1. This section needs to be amplified. Firstly, I would like a reference for the assumed standard deviation of 9.6mmHg. Second, are they referring to systolic or diastolic blood pressure? Thirdly, what is the justification for setting a non-inferiority margin of 10mmhg? Such a large difference between trial arms is almost inconceivable when one thinks that effective organisational interventions to improve control of BP (e.g. trials of self-monitoring of BP versus clinic monitoring) might achieve at best a difference between trial arms of 4 or 5mmhg. Even a small difference of say 2mmg Hg would have meaningful health impacts in terms of future heart attacks and strokes, therefore they need to set a much smaller minimum clinically important difference as the non-inferiority margin, which would require a much larger trial. However, its clear at various points in the protocol that the authors view this is as pilot study for a later subsequent trial. I would therefore suggest that they specify pilot study in the title and abstract. With regard to item 5d on the spirit checklist the applicants do not have an advisory group, trial steering committee or data monitoring committee. They say this is not necessary but I disagree. I think they should have some sort of committee external to the applicants to ensure independent oversight. Although data safety and monitoring are subject to audit by the institutional review board, I do not think this is sufficient and a steering committee or data monitoring committee specific to this trial is needed.

	The protocol does not specify any dates for the study. Has patient enrolment begun? If so, the date recruitment started should be specified. If not, the intended dates of recruitment should be stated. Spirit item 19: The applicants state on p14, lines 36-38 that data will be reviewed regularly for accuracy, completeness and reliability. I think the authors should give a bit more detail about how they will check these things. Spirit item 20b: The applicants do not mention any subgroup analysis and it would seem sensible to me that they do subgroup analysis by disease. This is particularly relevant given the fact that some of their outcomes are only applicable to patients with some chronic conditions. Spirit item 21a: As I've previously mentioned there is no proposal for a data monitoring committee. I think there should be such a committee and its role and independence should be specified in the protocol. Spirit item 25: There is no mention of how changes to the protocol will be managed and communicated. Spirit item 31c: It would be good to mention any arrangements for data sharing.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: Dr. Iñaki Martin Lesende
Institution and Country: Bilbao-Basurto Integrated Healthcare Organization (IHO), San Ignacio General Practice, Basque Health Service - Osakidetza, Bizkaia, Spain
Competing Interests: None declared

Comment:
This is a well-structured and interesting study as it will develop and evaluate an intervention using a practical ICT to cope with the increase of the elderly population and chronic diseases particularly in primary care. My main suggestions for the manuscript can be found below.

Response:
Thank you for your thoughtful comments and for the opportunity to refine our study protocol and improve our manuscript. Our responses to your suggestions are found below and we have revised our manuscript accordingly.

Comment:
In the ABSTRACT some aspects should be improved or better explained:
The patients included are not properly defined in this important section of the document.

Response:
Patients included in this study are those with stable well-controlled chronic disease, and with prior diagnoses of hypertension, hyperlipidemia, and/or diabetes. We have revised the 'Methods and analysis' section of the Abstract to define this more clearly.

Comment:

Only two primary outcome variables/measures are indicated, blood pressure (BP) and haemoglobin A1c (HbA1c) levels, as they were the most important outcome variables; however, there are non-diabetic patients where the control and results are not assessed through the HbA1c. This, as I will explain later, is a general drawback when explaining the outcome variables in the study.

Response:
Thank you for highlighting this aspect regarding the assessment of outcome variables in the study which can be better described.

The disease control of non-diabetic patients will be assessed through their blood pressure (BP) and low-density lipoprotein cholesterol (LDL-C) levels; while diabetic patients will be assessed through their HbA1c, BP and LDL-C levels.

We have revised the Abstract (Methods and analysis), Introduction (Study aims) and Methods (Study outcomes) sections of the manuscript to describe the outcome variables that will be evaluated for the different subgroups of patients - diabetics versus non-diabetics. We have also included LDL-C and disease control as additional primary outcome variables.

Comment:
In keywords, "healthcare kiosk" is not a mesh term; it could be changed by a mesh term?

Response:
We have changed it to a mesh term: “technology”.

Comment:
The STUDY AIM would be more understandable if it was presented in positive wording (instead of "... show non-inferiority ..."). And, included in the aim, the same considerations I made related to the main outcome measures, BP and HbA1c.

Response:
We have re-worded the sentence in the Study aims to “The aim of this follow-up study is to show equivalence of health outcomes for patients managed with the healthcare kiosk compared to the current standard of care.”.

We have also described more clearly the outcome variables that will be evaluated for the different subgroups of patients (diabetics/non-diabetics).

Comment:
METHODS
The setting should be better explained in this study (social and demographic characteristics, urban / rural setting, health support and network ...). Since only one health center is being evaluated, these characteristics are important to assessing its transferability and external validity.

Response:
The study will be conducted in a public primary care polyclinic (SHP – Punggol) which is located in the North-eastern region of Singapore. Sited within an urban setting adjacent to public housing estates, the polyclinic serves a growing population of about 146 640 multi-ethnic Asian residents.[1]

From a previous feasibility study,[2] our study population is expected to comprise mostly of patients in their fifth to seventh decade of life, to be of Chinese ethnicity, and have received secondary school education or lower.

For this study, the demographic data of recruited patients, such as age, gender, ethnicity, and education levels, will be recorded and analysed. As correctly highlighted, this will allow us to assess whether findings from this study are relevant to the general population with chronic diseases.

The study setting and the anticipated profile of recruited patients have been included in the manuscript (Methods – Study design).

Comment:
In the study, patients over 75 years are excluded though they represent a very important proportion of patients with chronic diseases. The reasons for this decision could be explained.

Response:
For this study, we have included patients up to 75 years of age. For patients above 75 years, the recommended levels for the clinical indicators of BP and HbA1c are less stringent than those currently coded in the kiosk decision algorithm. For example, for patients above 75 years of age, HbA1c levels of up to 8% are acceptable; and for those above 80 years of age, blood pressures of up to 150/90 mmHg are acceptable.

Should the kiosk be adopted into routine clinical practice following this study, the decision algorithm will be revised and expanded to allow for the inclusion of patients above 75 years of age.

The reason for selection of the age range in the inclusion criteria, has been added into the manuscript (Methods – Study population).

Comment:
The main outcome variables could be reconsidered or better explained. BP and HbA1C are indicated as the main ones. However, the clinical attitude and control are subsequently based on risk stratification and different variables depending on whether or not they are diabetic patients; for example, LDL levels are important in the latter. It might be more convenient to evaluate the degree of control (well, sub-optimally, and poorly - controlled) as the main outcome variable?. A stratified sample could also have been applied according to being diabetic or not in order to better consider and assess the outcome variables. This would also modify the estimated sample size.

Response:
The overall degree of disease control (well-, sub-optimally, poorly-controlled) is a composite measure of control of the individual outcome variables (BP, LDL-C, HbA1c). We acknowledge that its evaluation is useful and, guided by your recommendation to assess it as a primary outcome variable, we have made the necessary changes in the study protocol and manuscript.

Nonetheless, evaluating the individual outcome variables (BP, LDL-C, HbA1c) separately may allow us to detect subtle differences in control between intervention and control groups, and to identify which variable (BP, LDL-C or HbA1c) may be the more likely cause of any deterioration in overall disease control.

The evaluation of the individual outcome variables will be applied to the relevant stratified samples (diabetics and non-diabetics). For patients with diabetes, control of BP, LDL-C and HbA1c will be evaluated; for patients without diabetes, control of BP and LDL-C will be evaluated. We have made changes to the relevant sections in the manuscript to reflect the above (Abstract – Methods and analysis, Introduction – Study aims, and Methods – Study outcomes and Analysis).

Please note that the section on sample size estimation has been modified following another reviewer's comments. The sample size that we have chosen is based on a realistic estimation of the

number of patients that can be recruited from our study site, taking into consideration patient visits, operational constraints, and study timeline. As a rough estimate from our previous study, we recruited at a rate of 1 to 3 patients per day. The recruitment phase for this study is planned over 80 days, giving us an estimated recruitment of 80 to 240 patients. We realise this sample size limitation; however our study will serve as a pilot for a subsequent larger multi-center trial, with longer term follow-up. It will enable us to better establish the power calculations and evaluate the financial and logistic feasibility of a full-scale study.

Comment:
FIGURE 3 is partially unfocused, it could be improved.

Response:
We have improved the quality of the figure and revised it to show representative screenshots of the kiosk graphical user interface.

Comment:
The pathologies indicated in TABLE 1 and those indicated in the text in the inclusion do not coincide.

Response:
We have refined the inclusion criteria to patients with at least one chronic medical condition that includes hypertension, hyperlipidemia, diabetes mellitus. However, patients with other co-morbidities such as ischemic heart disease and stroke may also be included in the study. We have clarified this in the manuscript (Methods – Study population).

The medical conditions listed in Table 1 include any condition that will result in patients being classified into “Very high” or “High” risk groups that will subsequently impact upon their targets for disease control. Patients recruited into the study may or may not have any of these other co-morbidities, in addition to at least one of the 3 listed in the inclusion criteria.

Comment:
Considering a level of HbA1c <7 as good control might be very rigid for diabetic patients with certain characteristics (comorbidity or duration of the disease, according to recent clinical practice guidelines).

Response:
We recognise that stringent control of BP and HbA1c levels may not be relevant or safe for certain categories of patients such as the elderly. From our clinical practice guidelines, for patients above 75 years of age, HbA1c levels of up to 8% are acceptable; and for those above 80 years of age, blood pressures of up to 150/90 mmHg are acceptable. These recommended ‘cut-offs’ may be further modified depending on the patient’s profile e.g. frailty or life-expectancy. Hence for this study, we have chosen to include patients of up to 75 years of age only.

Comment:
It is indicated that HbA1c is measured in a diabetic patient with a capillary blood sample. How is it measured for those patients who use the healthcare kiosk?

Response:
All patients with diabetes will have their HbA1c levels measured from capillary blood samples taken at an on-site laboratory in the clinic. Samples will be analysed using a point-of-care device with results available in 6 minutes. This test will be done just prior to each kiosk usage or nurse consultation, for patients in the intervention and control groups respectively. We have added this description into the manuscript (Methods – Study outcomes).

Comment:
Some assessment should be made referring to specific costs, including the cost of the technology (healthcare kiosk and its maintenance).

Response:
A detailed evaluation of cost-effectiveness of kiosk versus routine clinic reviews will be done in a future follow-up study, as a larger multi-center trial with longer term follow-up will allow for these cost implications to be better appreciated.

Best regards and good luck.
Thank you for your review.

References
1. Singapore Department of Statistics. Population trends. 2017. http://www.singstat.gov.sg/publications/publications-and-papers/population-and-population-structure/population-trends
2. Ng G, Tan N, Bahadin J, et al. Development of an automated healthcare kiosk for the management of chronic disease patients in the primary care setting. J Med Syst 2016;40:169.

Reviewer: 2
Reviewer Name: Chris Salisbury
Institution and Country: University of Bristol, UK

Comment:
Thank you for asking me to review this trial protocol. I have tried to highlight issues which may need more clarification or justification in the protocol and other things which it may not be too late to change. When mentioning page numbers this relates to the numbers at the top of the combined PDF from BMJ Open.

Response:
Thank you for your time in reviewing our study protocol and for your important comments on our manuscript. Our responses are found below and we have revised our manuscript accordingly.

Comment:
I recommend the authors consider a more sophisticated approach to analysis using linear and logistic regression for continuous and categorical variables respectively, taking into account any variables which are unbalanced at baseline.

Response:
Thank you for your suggestions on the analysis. Following your recommendation, we shall be using linear and logistic regression analyses for the continuous and categorical variables respectively. We have modified the Abstract (Methods and analysis) and Analysis sections of the manuscript accordingly.

Comment:
The authors may wish to explain more about their choice of inclusion criteria in relation to their choice of outcome measures. For example, they are including people with hyperlipidemia and coronary heart disease who are not hypertensive or diabetic at baseline. I cannot see how HBA1C can be used as a primary outcome measure for people who are not diabetic but perhaps that's not the intention. Perhaps the applicants only intend to use HBA1C as an outcome measure in those who are diabetic.

Although BP is a relevant outcome for all of the diseases which form the inclusion criteria it would be surprising if it changes much in people who are well controlled at outset and in whom hypertension was not their problem. Perhaps the applicants could explain how they will combine BP and HPA1C in a population not all of whom are diabetic or hypertensive.

Response:
Thank you for highlighting this aspect regarding the inclusion criteria for medical conditions and the choice of outcome measures to be assessed, which needs to be better described.

We have refined the inclusion criteria to patients with at least one chronic medical condition that includes hypertension, hyperlipidemia, diabetes mellitus. Patients with other co-morbidities such as ischemic heart disease and stroke may also be recruited for the study, so long as they have at least one of the 3 listed conditions.

The evaluation of the individual outcome measures (BP, low-density lipoprotein cholesterol (LDL-C), HbA1c) will be applied to stratified samples - diabetics and non-diabetics. For patients with diabetes, control of BP, LDL-C and HbA1c will be evaluated; for patients without diabetes, control of BP and LDL-C will be evaluated.

We have revised the Abstract (Methods and analysis), Introduction (Study aims), and Methods (Study outcomes and Analysis) sections of the manuscript to describe more clearly the outcome measures that will be evaluated for the different subgroups of patients.

Although a patient may not have hypertension listed as one of their diagnoses, e.g. in a patient with diabetes and hyperlipidemia only, good BP control for any patient remains important. For a patient with chronic disease, all relevant disease targets need to be maintained and monitored regularly, as these conditions have a tendency to co-exist (metabolic syndrome).

Please note that we have included overall disease control (well-, sub-optimally, poorly-controlled) and LDL-C as additional primary outcome measures. Overall disease control is a composite measure of control of the individual outcome measures (BP, LDL-C, +/- HbA1c) that are relevant to the patient's diagnoses. The analysis of overall disease control will be applied to the entire patient cohort without subgrouping.

Evaluation of the individual outcome measures (BP, LDL-C, HbA1c) remains useful as it may allow us to detect subtle differences in control between intervention and control groups, and to identify which variable (BP, LDL-C or HbA1c) may be the more likely cause of any deterioration in overall disease control.

Comment:
It would be helpful if they could explain somewhere in the protocol when in the process patients have their blood taken, given that the results of these tests feed into the decision about whether or not they can collect their medication. Do they have the blood taken and analysed just before the kiosk visit?

Response:
LDL-C levels will be measured from fasting blood samples taken at baseline and just prior to the final study visit. These tests will be done at an on-site laboratory in the clinic. For patients with diabetes, HbA1c will be measured from capillary blood samples that will be obtained via finger-pricks, and analysed using a point-of-care device, with results available within a few minutes. This test will be done just prior to each kiosk usage or nurse consultation, for patients in the intervention and control groups respectively. We have added this description into the 'Methods – Study outcomes' section of the manuscript.

Comment:
The applicants say that the accuracy of the kiosk measurements will be verified (p12, line 19). Could they explain how they will do this verification?

Response:
Following each kiosk usage, kiosk measurements and decisions will be verified by a research coordinator. BP readings will be verified with repeat measurements taken using a validated automated digital BP monitor. Kiosk decision accuracy will be verified by checking the patient's parameters and laboratory results against the decision algorithm (table 2 of the manuscript) to ensure that the patient has been correctly classified. We have added this description into the 'Methods – Kiosk evaluation and triage' section of the manuscript.

Comment:
The applicants state on p11, line 20 that people who have suboptimal or poorly controlled disease will be taken out of the study and attend routine clinic consultations for their subsequent follow up visits and yet on p14, line 37 they say the study will be analysed by intention to treat. If they take patients out of the study who have poorly controlled disease then by definition the only people remaining in the study at the end will be those with well controlled disease and equivalence between the study arms is guaranteed. It may be appropriate that people with suboptimal control are taken out of kiosk care and followed up through clinic consultation, but following the intention to treat principle its very important that they stay in the analysis. Keeping people with poor control in the analysis to the end applies to both arms of the trial.

Response:
We note the above contradiction and have made the necessary corrections to the manuscript (Methods – Kiosk evaluation and triage). Patients with sub-optimal or poorly-controlled disease will be taken out of kiosk care but will be kept in the analysis for the study. Analyses will be applied to all patients recruited for the study.

Comment:
This seems a very small study but the reason for this becomes clear when one looks at the power calculation. The authors have assumed a standard deviation in BP of 9.6 and a noninferiority margin of 10, i.e. an effect size of more than 1. This section needs to be amplified. Firstly, I would like a reference for the assumed standard deviation of 9.6mmHg. Second, are they referring to systolic or diastolic blood pressure? Thirdly, what is the justification for setting a non-inferiority margin of 10mmhg? Such a large difference between trial arms is almost inconceivable when one thinks that effective organisational interventions to improve control of BP (e.g. trials of self-monitoring of BP versus clinic monitoring) might achieve at best a difference between trial arms of 4 or 5mmhg. Even a small difference of say 2mmg Hg would have meaningful health impacts in terms of future heart attacks and strokes, therefore they need to set a much smaller minimum clinically important difference as the non-inferiority margin, which would require a much larger trial. However, its clear at various points in the protocol that the authors view this is as pilot study for a later subsequent trial. I would therefore suggest that they specify pilot study in the title and abstract.

Response:
The assumed standard deviation of 9.6mmHg for systolic BP (SBP) was calculated from the patient cohort in a previous feasibility study.[1]

We note that the assumption of a non-inferiority margin of 10 mmHg is too large to be clinically meaningful. As the mean SBP of the study participants in our previous study was 126 mmHg, we assumed that a rise/difference of 10 mmHg or more in the mean SBP might be indicative of a shift in

SBP of most participants to an out-of-target value (>140 mmHg), signifying poor disease control. We realise that this assumption is erroneous, and to be clinically relevant we should have set a non-inferiority margin of 4 to 5 mmHg. We acknowledge that this has resulted in a much larger sample size estimation.

The sample size that we have chosen to work with (120) is based on a realistic estimation of the number of patients that can be recruited from our study site, taking into consideration patient visits, operational constraints, and study timeline. As a rough estimate from our previous study, we recruited at a rate of 1 to 3 patients per day. The recruitment phase for this study is planned over 80 days, giving us an estimated recruitment of 80 to 240 patients. We have made the necessary changes to the Analysis section of the manuscript to reflect the above.

We recognise the limitation of a small sample size; however this study will serve as a pilot for a subsequent larger trial with longer term follow-up. It will enable us to better establish the power calculations and evaluate the financial and logistic feasibility of a full-scale study. We note your suggestion to specify it as a pilot study and we have indicated this in the Title and Abstract of the protocol.

Comment:
With regard to item 5d on the spirit checklist the applicants do not have an advisory group, trial steering committee or data monitoring committee. They say this is not necessary but I disagree. I think they should have some sort of committee external to the applicants to ensure independent oversight. Although data safety and monitoring are subject to audit by the institutional review board, I do not think this is sufficient and a steering committee or data monitoring committee specific to this trial is needed.

Response:
The study protocol was presented recently to an independent advisory committee, comprising representatives from the Departments of Clinical Services and Operations, Finance, Nursing, Pharmacy and Information Technology (Integrated Health Information Systems – IHiS). Members of this committee will not be directly involved in the trial and will be free to review any information or study process related to the trial. The committee will be updated on trial progress at quarterly intervals and will give recommendations for discontinuation, modification or continuation of the study. We have included this into the manuscript (Methods – Data management and monitoring).

Comment:
The protocol does not specify any dates for the study. Has patient enrolment begun? If so, the date recruitment started should be specified. If not, the intended dates of recruitment should be stated.

Response:
Patient enrolment has not begun. We intend to start patient recruitment in March 2018. This has been added in the manuscript in the section 'Methods – Recruitment and randomisation'.

Comment:
Spirit item 19: The applicants state on p14, lines 36-38 that data will be reviewed regularly for accuracy, completeness and reliability. I think the authors should give a bit more detail about how they will check these things.

Response:
We have elaborated further on this aspect in the manuscript (Methods – Data management and monitoring). Data collection forms will be checked fortnightly by the PI and research coordinator for completeness and accuracy (including range checks, missing data and double-entry). Physical and

digital records will be cross-checked for consistency. A research executive from the SHP Department of Research will audit every participant's records 3-monthly to ensure that record keeping meets regulatory requirements and is kept up-to-date.

Comment:
Spirit item 20b: The applicants do not mention any subgroup analysis and it would seem sensible to me that they do subgroup analysis by disease. This is particularly relevant given the fact that some of their outcomes are only applicable to patients with some chronic conditions.

Response:
The evaluation of outcome measures will be applied to stratified samples as previously described, and we have updated the manuscript and Spirit Checklist to reflect this.

Comment:
Spirit item 21a: As I've previously mentioned there is no proposal for a data monitoring committee. I think there should be such a committee and its role and independence should be specified in the protocol.

Response:
An independent advisory committee will be updated on trial progress at quarterly intervals and will give recommendations for discontinuation, modification or continuation of the study. We have added this into the manuscript (Methods – Data management and monitoring) as previously described.

Comment:
Spirit item 25: There is no mention of how changes to the protocol will be managed and communicated.

Response:
Any modification to the study protocol will be communicated to the CIRB, trial advisory committee, study team members and trial participants. The CIRB will be informed of any protocol change via an online CIRB Amendment Form and any change will be implemented only after approval has been obtained. The advisory committee and study team members will be informed of any change to the protocol via email or in person. Trial participants will be informed of any change to the protocol via phone or in person.

We have added this into the manuscript (Ethics and Dissemination – Research ethics approval) and updated the Spirit Checklist accordingly.

Comment:
Spirit item 31c: It would be good to mention any arrangements for data sharing.

Response:
Following study completion and publication of findings, all data will be deposited in an appropriate data archive for sharing purposes and will be made freely available upon request to the corresponding author. We have added this into the manuscript (Ethics and Dissemination – Dissemination of study findings) and updated the Spirit Checklist accordingly.

Reference

1. Ng G, Tan N, Bahadin J, et al. Development of an automated healthcare kiosk for the management of chronic disease patients in the primary care setting. J Med Syst 2016;40:169.

VERSION 2 – REVIEW

REVIEWER	Dr. Iñaki Martin Lesende San Ignacio Health Centre, Bilbao-Basurto Integrated Healthcare Organisation (IHO), Basque Health Service (Osakidetza), Spain
REVIEW RETURNED	23-Jan-2018

GENERAL COMMENTS	The authors have made important modifications to the manuscript following all the recommendations of the reviewers. The document has improved considerably, and I only give some last recommendations to be taken into account. These are: The TITLE could be shorter, i.e. deleting "Evaluating the ..." or "study". It could be: Health outcomes of patients with chronic diseases managed with a healthcare kiosk in primary care: protocol for a pilot randomised controlled trial. In ABSTRACT, STUDY AIMS and METHODS, I consider the main outcome variable is the "overall chronic disease control" determined through the other result variables (BP, LDL-C, Hb A1c). METHODS AND ANALYSIS Ineligible patients are exclusión criteria too. Stratification in the randomization of the sample will not be applied, although this would help to have enough patients for each group and obtain a more balanced sample. It could be considered. The section "Sample size estimation" could be better located after "study population" than in the "Analysis" section (this section more related to the data analysis itself). The multivariate analysis could be described more in detail, indicating the method used for logistic regression, dependent and independent variables, ... The final part "12 months after recruitment" in FIGURE 1 is not well understood. Some REFERENCES could be omitted, for example the 11, as they indicate concepts that are widely known and accepted. OTHER GENERAL CONSIDERATIONS The study is quite restrictive with the patients included in terms of age, disease control and other characteristics. It is important to highlight this, with the possibility of contrasting the results applying the methods to other types of patients in the future. Patients, at least in this pilot study, are not so autonomous in the process of interaction with the healthcare kiosk, since they are supervised by the research coordinator and they need to contact a laboratory technician to obtain the hbA1c in case of being diabetic. Although perhaps it is considered in later studies, I think it is important to comment costs / cost-effectiveness aspects in the application of this technology.

	Congratulations on the article in this final state of review. Best regards

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: Dr. Iñaki Martin Lesende
Institution and Country: Bilbao-Basurto Integrated Healthcare Organization (IHO), San Ignacio General Practice, Basque Health Service - Osakidetza, Bizkaia, Spain
Competing Interests: None declared

Comment:
The authors have made important modifications to the manuscript following all the recommendations of the reviewers. The document has improved considerably, and I only give some last recommendations to be taken into account. These are:

Response:
We thank our reviewer for his positive comments and further recommendations. Our responses are found below and we have revised our manuscript accordingly.

Comment:
The TITLE could be shorter, i.e. deleting "Evaluating the ..." or "study". It could be: Health outcomes of patients with chronic diseases managed with a healthcare kiosk in primary care: protocol for a pilot randomised controlled trial.

Response:
We have shortened the title as recommended by our reviewer.

Comment:
In ABSTRACT, STUDY AIMS and METHODS, I consider the main outcome variable is the "overall chronic disease control" determined through the other result variables (BP, LDL-C, HbA1c).

Response:
We agree with our reviewer on this aspect and have made the relevant changes to the manuscript to reflect this (Abstract – Methods and analysis, Introduction – Study aims, and Methods – Study outcomes).

We describe overall chronic disease control as the main primary outcome variable that will be evaluated for all patients. The evaluation of the other outcome variables will be applied to the relevant stratified samples (diabetics and non-diabetics).

Comment:
Ineligible patients are exclusion criteria too.

Response:

Patients with one or more of the listed exclusion criteria are ineligible for the study and will be excluded from recruitment. We have rephrased the description in the 'Methods – Study population' section for greater clarity.

Comment:
Stratification in the randomization of the sample will not be applied, although this would help to have enough patients for each group and obtain a more balanced sample. It could be considered.

Response:
Following our reviewer's suggestion, we shall be applying stratification in the randomisation using diabetic and non-diabetic subgroups, as described in the 'Methods – Recruitment and randomisation' section.

Comment:
The section "Sample size estimation" could be better located after "study population" than in the "Analysis" section (this section more related to the data analysis itself).

Response:
We have moved the section from the 'Analysis' section to the 'Methods' section as recommended by our reviewer.

Comment:
The multivariate analysis could be described more in detail, indicating the method used for logistic regression, dependent and independent variables, ...

Response:
We have elaborated further on the multiple regression models that will be used for the analysis. After adjusting for patient age, gender, ethnicity and education level (independent variables), the effect of the intervention will be analysed with the primary outcome variables (overall disease control, BP, LDL-C, HbA1c) as the dependent variables. The effect of the intervention over time will be examined using mixed-design analysis of variance, with intervention as the between-subject factor and time as the within-subject factor.

Comment:
The final part "12 months after recruitment" in FIGURE 1 is not well understood.

Response:
We have replaced this with 'End of study' for greater clarity.

Comment:
Some REFERENCES could be omitted, for example the 11, as they indicate concepts that are widely known and accepted.

Response:
We have omitted Reference 11 as recommended by our reviewer.

Comment:
The study is quite restrictive with the patients included in terms of age, disease control and other characteristics. It is important to highlight this, with the possibility of contrasting the results applying the methods to other types of patients in the future.

Response:
We recognise this study limitation with regards to patient age, disease diagnoses and control. However, the study shall serve as a pilot for subsequent studies of wider scope.

Future studies may explore the management of patients above 75 years of age who are an important group of patients with chronic disease.

For disease types, we may consider including stable patients with the following disease conditions: hypo- or hyperthyroidism, asthma, and COPD, who can be monitored with the relevant disease indicators.

We can also explore kiosk usage in the co-management of patients with sub-optimally controlled disease, who may benefit from initial lifestyle advice and modifications.

We have elaborated on these limitations and potential future directions of the study in the 'Discussion' section of the manuscript.

Comment:
Patients, at least in this pilot study, are not so autonomous in the process of interaction with the healthcare kiosk, since they are supervised by the research coordinator and they need to contact a laboratory technician to obtain the hbA1c in case of being diabetic.

Response:
As we are exploring a new method of care delivery, a certain degree of guidance and direction is required for the initial phase. With regular kiosk usage over time however, we anticipate greater patient confidence and autonomy, as was observed in our feasibility study.[1] The eventual aim is for the deployment of a self-service healthcare kiosk, that will allow for its full benefits to be realised in terms of patient empowerment and resource allocation. These may be better appreciated in a longer-term follow-up study.

With further technological advancements in medical devices, we hope to incorporate other point-of-care devices into the kiosk, that might include the non-invasive measurement of HbA1c.

We have included these further considerations in the 'Discussion' section of the manuscript.

Comment:
Although perhaps it is considered in later studies, I think it is important to comment costs / cost-effectiveness aspects in the application of this technology.

Response:
We have expanded the 'Discussion' section of the manuscript to include a description of the cost assessments that may be considered in the application of the kiosk in clinical care.

Comment:

Congratulations on the article in this final state of review.

Thank you very much for your valuable inputs.

References

1.Ng G, Tan N, Bahadin J, et al. Development of an automated healthcare kiosk for the management of chronic disease patients in the primary care setting. J Med Syst 2016;40:169.

VERSION 3 – REVIEW

REVIEWER	Dr. Iñaki Martin Lesende Bilbao-Basurto Integrated Healthcare Organization (IHO), San Ignacio General Practice, Basque Health Service - Osakidetza, Bizkaia, Spain
REVIEW RETURNED	06-Feb-2018

GENERAL COMMENTS	The authors have made modifications in the manuscript based on all my comments. I have only missed something more explicit data about costs (device and maintenance). Therefore, the article is suitable for publication.. Congratulations!