We thank both Reviewer 1 and Dr. Jones for their very thoughtful and detailed comments. The authors have consequently carefully revised the manuscript.

**COMMENTS FROM DR JONES**

**Thank you for taking this study on. It is an important clinical question to pose. Having worked in post-op ICU care of cardiac surgery patients for > 10 years, I often wondered the strength of the evidence to push patients' K levels over 4. Therefore, your ultimate RCT will be of enormous interest to the global medical community.**

We are grateful for these kind words.

**It was unclear to me whether the patients enrolled in the feasibility pilot will become part of the dataset for the full RCT, or if their inclusion into the full dataset would be contingent upon some constraint(s) (such as no material protocol changes). Please clarify this in the manuscript.**

This is an excellent point. This is a feasibility study and, following the NIHR guidelines, is being run before main study in order to answer the question “Can this study be done?”. Our primary outcomes are feasibility outcomes and whilst we are collecting indicative outcome measures these will be used to refine the outcomes for the main trial and estimate necessary parameters. They will also be seen by investigators. We therefore do not propose to combine them with the data from the proposed main trial.

<https://www.nihr.ac.uk/funding-and-support/documents/funding-for-research-studies/research-programmes/RfPB/FAQs/Feasibility_and_pilot_studies.pdf>

**I was curious about the phrase "'Atrial Fibrillation' will be defined as an episode of AF lasting ≥30 seconds that is clinically detected and/or electrocardiographically confirmed". This implies to me that anybody taking care of the patient could state that the patient had 30s of a. fib. and then this would qualify as meeting the criteria (even without ECG confirmation) for your study. Was this your intention? If so, who would qualify to detect this event: ICU nurse? MD only?**

We welcome this question, and are delighted to respond.

This was the result of extensive discussions. We tried to choose a pragmatic definition well suited to a ‘real-world study’ where arrhythmias are occasionally identified without an ECG recording for post-event confirmation. We recognize that such episodes may be identified in our study without an ECG recording but all arrhythmia diagnoses will be confirmed using Holter monitoring that will occur in parallel (see below).

**P10: "vice versa"**

Thank you for pointing out this error. We have opted to amend the text for greater , as follows:

“*A patient from the ‘Relaxed’ group being treated as if they are in the ‘Tight’ Group, or a patient from the ‘Tight’ group being treated as if they are in the ‘Relaxed’ Group.”*

”

**P11: item 7. How will "cost effectiveness" be determined?**

We are grateful that the need for further clarification has been pointed out. We plan to undertake detailed analysis of cost-effectiveness in the future final study but are not funded to undertake a full cost-effectiveness analysis during this pilot study. However, we will be collecting some soft measures of cost-effectiveness here, including length of stay and quality of life analyses that will enable some simple statistical analyses to be undertaken.

As a consequence, the following text has been added to the Statistical analysis section:

*“A detailed cost-effectiveness analysis will not be undertaken in this pilot trial, but simple analyses of cost-effectiveness will be performed utilizing data relating to quality of life and length of stay.”*

**P11: "Episodes of clinically-identified 'AF' (as well as other arrhythmic events identified) will be confirmed." What does "be confirmed" actually mean?**

We apologise for our lack of clarity. In response, he text has been modified as follows:

“*The time of all clinically-identified episodes of AF will be documented and contemporaneous Holter monitoring recordings will be reviewed to confirm or deny the AF diagnosis after Day 5 by clinical staff blinded to treatment allocation*.”

**The non-inferiority margin of 10% (I presume this is absolute and it should be explicit) seems very high. As a clinician, I personally would not see 35% incidence and 45% incidence as being "non-inferior". I would definitely consider 45% to be clearly inferior.**

We welcome the chance to offer clarification on this issue.

The reported incidence of AF following cardiac surgery ranges from 10%-65%. (doi: 10.4103/1995-705X.73212) and remains controversial. The values of a 35% baseline incidence with a 45% non-inferiority incidence were chosen on pragmatic grounds. A smaller difference between these percentages would require significantly many more patients to be recruited for the study to be adequately powered, and would make it unfeasible to fund and undertake. The clinical question could therefore not be answered at all. However, we acknowledge this reasonable concern from the editor. When the final study is undertaken, if the final percentages are actually 35% and 44%, although the statistical analysis will state that there is no difference between the groups, a more nuanced qualification will be required in the final manuscript.

**Could you reference the sample size equation used? Commonly is [https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2351444/pdf/bmj00549-0040.pdf](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2351444/pdf/bmj00549-0040.pdf" \t "_blank), but certainly not always. I could not replicate the sample size.**

We apologies for the confusion surrounding the proposed sample size calculations for the main trial. We have edited the text to clarify that the proposed sample size is in fact 1682 and that the one sided alpha is 2.5% corresponding to a two sided alpha of 5%. The original figure of 1770 was 20% of the eligible (as targeted by our feasibility study) but we can see that this is misleading.

The formula used was

n = f(α, β) × [πs × (100 − πs) + πe × (100 − πe)] / (πs − πe − d)2

where πs and πe are the true percent 'success' in the standard and experimental treatment group respectively, and f(α, β) = [Φ-1(α) + Φ-1(β)]2

**REVIEWER 1:**

We thank the reviewer for his/her helpful and constructive comments. We are happy to respond, and are in no doubt that the manuscript has benefitted as a result.

Specifically, they make a large number of comments regarding clarity, consistency and punctuation, which we have endeavored to address. References have been added where advised.

With regards to the need for additional data: the comments made will no doubt help improve the future full study. However, respectfully, they do not have a strong bearing on this feasibility study for which this particular manuscript describes.

**Title Page. The title is slightly different from the abstract and the text where it says "Tight K pilot: a randomized..." In the text the authors mention "TIGHT-K pilot trial".  Please be consistent in wording.**

**and**

**Page 4, line 15/ The TIGHT-K pilot trial... The authors could be more consistent with wording. The title refers to the Tight-K pilot, whereas here it says the TIGHT-K pilot trial. Please choose one to be used in the entire manuscript.**

We have revised the manuscript to ensure consistency and have used “Tight K” or ‘Tight K Pilot’ throughout. Specifically, the Discussion in the Abstract has been amended to refer to ‘Tight K pilot’ (without capitals or a hyphen).

**Page 5, line 4: [AF]), this seems to be a typo, should probably read (AF) instead of brackets.**

We apologise for this error. The text has been amended as follows:

Approximately one in three patients is affected by atrial fibrillation (AF) after cardiac surgery …

**Page 5, line 17 please provide a reference to the statement that AF incidence is higher in the elderly.**

The reference has been added as requested.

**Page 6, line 5. The authors claim that central venous access is maintained for the purpose of potassium supplementation. Is this really true?**

This is indeed often the case, this reflecting the view of our Trial’s Protocol Development Group, which consists of cardiac intensivists, cardiologists and cardiac surgeons.

**Page 6, Line 7. The authors state that in cardiothoracic units the most expensive drug is IV potassium. This seems a very bold statement. Could you perhaps provide some reference/supplemental material?**

This is indeed true. Although the individual unit costs would not be perceived as expensive, the total costs are high due to its very extensive use. We have provided a reference to our local audit data, which was included on the clinicaltrials.gov submission.

**Page 6, Line 30 duplicated word "after"**

We apologise for this error, and the text has been amended accordingly.

**Page 7, line 55: exclusion criterion 9 is not published on [clinicaltrials.gov](http://clinicaltrials.gov/" \t "_blank)**

We thank the reviewer for pointing out this discrepancy regarding the exclusion data and apologise for our oversight. We will amend clinicaltrials.gov to add exclusion criterion 9 “Unable to give informed consent”

**Page 8, line 2: The proposed first step in obtaining informed consent seems to be to provide eligible patients with an information sheet. However, is that the correct order? Should not the most responsible physician in charge consent too? So in case of approaching, should it not be that 1) the first point of patient contact must be from someone within the patient's circle of care, ie. the patient is seen by their more responsible physician (the surgeon) and informed that they can be approached by a member of a research team, who 2) will inform them of an ongoing study? Only after, or during that meeting 3) the patient will be provided with an information sheet.**

**And**

**Page 8, line 10: Is research staff indeed allowed to pre-screen eligibility of patients and approach them before the most responsible physician does? If the investigator or his/her staff are pre-screening for eligibility to which they are not the patients physician and not considered within the patient's circle of care, the investigator would first need to obtain permission from the most responsible care provider to pre-screen patient charts. The investigator can assign their staff or affiliates to pre-screen those patients' charts to identify potential research participants. The staff or affiliates that have been assigned to pre-screen charts to identify potential research participants do not have to be within the circle of care as long as the investigator has obtained permission to pre-screen those charts from the most responsible care provider who is within the circle of care.  
Furthermore, there should be written documentation of this approval (e.g., dated/signed log) where the most responsible care provider(s) confirm that the PI and or their research staff for the study has been delegated right to access to pre-screen for potential eligibility.**

These remarks may represent the Reviewer’s own local cultural research practice and this may not necessarily reflect the process of recruitment in many cardiothoracic surgical and cardiothoracic critical care studies elsewhere. The authors confirm that in the institutions where recruitment will occur, all responsible clinicians and cardiac surgeons in the department have granted unit-wide approval for their own eligible patients to be approached. The protocol including all aspects of recruitment has been fully approved by a national ethics committee (under the auspices of the United Kingdom NHS Health Research Authority).

**Page 8, Line 20. With respect to the 24h hour period for consideration/reflection, what happens with same day admit patients? Are they not eligible for the study? If so, should that be an additional exclusion criteria? Or are all cardiac patients admitted the day before surgery?**

We thank the reviewer for their query. We have ethical approval that states that patients will be offered at least 24 hours to decide whether they would want to take part in the study. All patients for elective CABG are admitted the day before and due to our inclusion criteria, we are not recruiting emergency patients. However, if patients are happy to give informed consent less than 24 hours after receiving the patient information sheet, then they may do so as long as the person taking consent is satisfied that the patient is making a fully informed decision.

**Page 8, line 32 "Eligible participants" Should that not be changed to 160 participants?**

The reviewer is correct. The text has thus been amended as follows:

“*One hundred and sixty eligible participants with informed written consent will be allocated…”*

**Page 8, line 32 Who is performing the randomization? How will all people involved in the care of the patient be made aware of the study? How do the authors ascertain that there is no protocol violation at night when they are not present?**

We thank the reviewer for their queries.

Randomisation is through an online database (<https://sealedenvelope.com/>). Trained staff sign a delegation log and they are given unique log in access to the randomisation website. After consent has been obtained, the trained personnel at the hospital sites (mainly nursing staff with permission from the local R&D department and the Principal Investigator) will login to provide entry details and receive the allocation. A SOP is also provided with further information on the randomisation process.

Promotion and training of staff has taken place before the Tight K trial was opened to recruitment at both of the hospitals sites. Promotional materials have been developed which includes stickers for notes, observational charts and posters.

Every measure has been taken to avoid protocol violations. Tight K wrist bands have been developed for the patients to wear whilst they are in hospital. The wrist bands show the group the patient has been randomised to. As the trial is unblinded the patients are also aware of their allocation where this is possible.

Training and explanations of the 2 different trial treatments has been given to all of the ITU staff so they are aware of the 2 treatment arms. Stickers have been produced which are attached to all observation charts, prescription charts and posters to be displayed where the patients are likely to be looked after.

**Page 8, line 40. I would not refer to the "treatment process" under the heading or "Randomization". Rather delete or rephrase as "The first part of figure 1 shows ..."**

We thank the reviewer for this helpful comment. In response, the following text has been moved to the start of the next sub-heading:

“*A flowchart of the trial treatment intervention process is shown in Figure 1*”.

**Page 8, line 47: Trial treatment, I would rather rename to Trial treatment period**

The text has thus been amended in line with the reviewer’s suggestion.

**Page 8, line 57. You could probably add that the follow up period lasts 28 days.**

This is stated in the methods section which follows.

***“28 days post-operative follow-up.***

Patients surviving to hospital discharge will be followed-up by telephone or post 28 days after randomisation to determine mortality and further episodes of heart rhythm problems (if known).”

**Page 9, line 1: I would rearrange the order of the following sections to  
-    Tight potassium control  
-    Relaxed potassium control  
-    Potassium supplementation  
-    New heading > routine clinical practice (original line 1 - 10)**

The text has thus been amended in line with the reviewer’s suggestion.

**Page 9, lines 17 and 25: I would probably reference to Figure 1 again. With respect to the figure, it seems that only the relaxed control arm will have AF diagnosed. Could you adjust the figure so that there is a line from both the "tight control" and the "relaxed control" boxes going to the "AF diagnosed" box?**

The authors have amended the figure as suggested.

Likewise, we have referenced the figure again, amending the text as follows:

**Routine clinical practice**

All other clinical practice (including the use of magnesium supplementation, the use of beta-blockers or anti-arrhythmic agents, the route of potassium administration, and blood tests) will be routine, and independent of trial allocation. In particular, the frequency with which serum [K+] is monitored will be according to existing protocols and clinician / nursing staff preference (Figure 1).

and

**Patients with AF**

In keeping with recognized international criteria, ‘Atrial Fibrillation’ will be defined as an episode of AF lasting ≥30 seconds that is clinically detected and/or electrocardiographically confirmed (on either a 12-lead electrocardiogram (ECG), telemetry[[20](#_ENREF_20" \o "Calkins, 2012 #130)]. Routine clinical monitoring will be supplemented by continuous Holter monitoring (eMotion Faros 180, Technomed Ltd) for the first 120 postoperative hours for all participants. Once a patient has a period of AF, which is clinically identified, the trial treatment period ends and then there will be no restriction on potassium supplementation and they should be treated according to current practice (Figure 1).

P**age 10, line 1: telemetry [18], the superscript here is not in keeping with the format of the other references.**

We apologise for this error. The formatting has been amended as suggested.

**Page 10, line 5: probably you want to rephrase this to "once a patient has ... AF, the trial has ended and further treatment is according to local/current practice".**

The text has been amended in response to the Reviewer’s helpful suggestion.

**Page 10, line 27: why is your primary aim not just "number of patients recruited in 6 months" as it says on [clinicaltrials.gov](http://clinicaltrials.gov/" \t "_blank)?**

**and**

**Page 10, line 47: From [clinicaltrials.gov](http://clinicaltrials.gov/" \t "_blank) it seems that your fourth primary aim is to collect data on the occurrence of outcomes. Possibly to secure your power analysis. This is slightly different form the fourth aim you present here.**

Thank you to the reviewer for pointing out this discrepancy.

On clinicaltrials.gov we say: “The primary purpose of this pilot study will be feasibility of recruitment”. What we have in the manuscript is a fuller version i.e. “Our primary aim is “to assess the feasibility and acceptability of planning and delivering the intervention and trial methods to inform a full-scale non-inferiority trial” i.e. it’s more than recruitment. So we agree that these are not quite congruent and we will amend the version on clinicaltrials.gov**.**

However, ‘Aims’ are not quite the same concept as ‘outcomes’. Our outcomes are feasibility of participant recruitment and randomization; maintaining a protocol violation rate <10%; and retaining 90% patient follow up 28-days after surgery. We think these are compatible with what we wrote on Clinical trials.gov i.e. the number of patients **recruited** over a 6 month period; number of patients successfully **randomised** into the study; feasibility of ensuring that **protocol violation** rate is no more than 10%; and feasibility of following up and obtaining outcome data for 90% of the patients randomised at 28 days. Therefore, we have not made any changes to the manuscript.

**Page 10, line 32: please be more specific on aim no 2. What do you mean by "possible". Perhaps you want to identify several potential problems:  
- The actual computer randomization (power failure, website failure, no member of the team available)**

**- Excluded from analysis before or after randomization because of cancelled or rescheduled surgery, elective surgery changing to urgent/emergency surgery  
- The protocol adherence in the critical care (different providers of care, new residents coming in for their rotation)**

**- Protocol adherence on the floor**

**- What to do if a patient is discharged early (within 120 hours)  
- What to do if you're short of Holter monitor or they fail**

**and**

**Page 10, line 40: it seems you're exclusively interested in cross over. Please adjust your wording accordingly. Protocol violations would be the ones I added above. Please rethink and rephrase.**

The authors agree with the reviewer’s thoughtful ideas about potential causes of randomization failure and have revised the manuscript.

We have described a number of potential causes of protocol violations after the primary endpoints:

Reasons for a protocol violation may include:

* A patient from the ‘Relaxed’ group being treated as if they are in the ‘Tight’ Group, or a patient from the ‘Tight’ group being treated as if they are in the ‘Relaxed’ Group
* Failure of randomisation
* Alteration in planned surgery
* Failure of Holter monitoring process
* Lack of data completion

Patient discharge before 120 hours would be not be considered a protocol violation. All of our endpoints in the manscript and on clinicaltrials.gov refer to ‘up to 5 days’ or ‘maximum 5 days’. However, we note that Figure 1 states “for 5 days” and we have accordingly amended this to “*up to 5 days*”).

**Page 11, line 5 and 7: what if the duration of stay is longer than 28 days, will you truncate the length of stay at 28 days? What does that mean for mean/median duration of stay you will be presenting?**

We thank the reviewer for this thoughtful query. The trial period will end at 28 days. Length of stay data will be collected for all patients in the study without truncation. In the full study, the numbers of patients with LOS>28 days will be small and it is very unlikely this will have a significant impact on overall mean/median values.

**Page 11, Line 10: for how long are you following patient for arrhythmia's? 28 days? Please add.**

We have amended the manuscript in order to clarify the fact that only arrhythmias detected up to 5 days (120 hours) will be included in the secondary endpoint. The adjusted text now reads,

“4. *Incidence and total duration of all other arrhythmias until Day 5 (120 hours), defined using standard diagnostic criteria.”*

**Page 11, line 20: Cost effectiveness is a very vague term. Please explain what you are going to collect: costs of Holter monitoring, medication, labs, cardiac diagnostics (ECG)? How do you define the benefits? What monetary value are you using for patient years/quality of life, etc?**

We are grateful that the need for further clarification has been pointed out. We plan to undertake detailed analysis of cost-effectiveness in the future final study but are not funded to undertake a full cost-effectiveness analysis in this pilot study. However, we will be collecting some soft measures of cost-effectiveness here, including length of stay and quality of life analyses that will enable some simple statistical analyses to be undertaken.

As a consequence, the following text has been added to the Statistical analysis section:

“*A detailed cost-effectiveness analysis will not be undertaken in this pilot trial, but simple analyses of cost-effectiveness will be performed utilizing quality of life data and length of stay data*.”

**Page 11, line 30: Did you confirm if the surgical team is interested in 120 hours of Holter monitoring results? Could it be they only want information on arrhythmia's?**

The purpose of the 120 hours of Holter monitoring is to (1) confirm arrhythmias that were detected clinically and (2) identify other arrhythmias. A copy of the report will be sent to the surgical team because they have ultimate clinical responsibility for the patient. The surgical teams in our recruiting centres are happy with all aspects of the protocol.

**Page 11, line 40: when will they complete the questionnaire before surgery? In pre admission? In the floor waiting for surgery? Still at home? Please specify. The answers could be slightly different when someone is fasting and anxious before surgery, as compared to being at home. Also, you probably want to add some information on the questionnaire to page.. [sic]**

We are grateful for the reviewer’s very valid points about the timing of the questionnaire completion.

For the purposes of the feasibility study, we want to assess our capability to successfully collect the questionnaire at any time prior to randomization. We accept that careful consideration will need to be given to the optimal time point for the unbiased collection of these data. Preliminary thoughts among the Protocol Development Group lean towards stipulating the collection of these data at the time of consent, but this will certainly require more careful consideration.

**Page 11, line 52: How to determine mortality of someone who lives alone? Could you perhaps change your sequence of contact? 1) hospital notes/most responsible physician notes, 2) contact person, 3) participant. Did you mention in your letter of informed consent that you could be contacting a first contact person?**

Determining mortality in the United Kingdom is a straightforward process and uses links to primary care records, hospital records and the UK official register of Deaths.

**Page 12, line 18: total number... Please add time frame.  
and**

**Page 12, line 21: please add time frame.**

We have amended the manuscript to reiterate that the study period is 6 months. The amended text now reads,

“*The following will be collated over the trial study period (6 months):”*

P**age 12, line 26: please rephrase to "cross over" instead of violations.**

We have amended the text accordingly.

**Page 13, line 1: You might want to add platelet aggregation inhibitors and not only anticoagulant drugs, you also might want to add statins, diuretics, atypical antihypertensives (such as clonidine, alpha blockers, etc). You also might want to record date and time of last dose before surgery.**

We are grateful for the reviewer’s thoughts on what data could be collected as part of the protocol. We opted not to collect these data for this feasibility study but will consider these points carefully when we embark on the future full study.

**Page 13, line 8: History of arrhythmia's [sic] seems to contradict exclusion criterion 7. Please explain.**

We thank the reviewer for their query. “Current or previous use of medication for the purposes of cardiac rhythm management “ is an exclusion criteria. We are also asking about a history of arrhythmias in the baseline clinical dataset. However, there is no discrepancy; rarely, patients are identified with silent arrhythmias on rhythm monitoring, when it is subsequently opted not to treat these with medication. The clinical history we obtain would identify this low numbers of patients.

**Page 13, line 8 You might want to add peripheral vascular disease and smoking**

Regarding additional data - again we are grateful for the reviewer’s comments and will consider this point carefully for the future full study.

**Page 13, line 18: where do you collect your data from? TTE, TEE, CT? Why would you choose to define MV pathology as moderate or worse, and not as normal/mild/moderate/severe? Do you think that a dilated RV or RA (with pulmonary hypertension, TV or PV pathology) could also lead to AF? Should you collect data on right heart pathology too?**

As above – we will consider the reviewer’s helpful comments for the full future study. We are only collecting data for MV disease that is moderate or worse, as the Protocol Development Group does not believe that mild mitral valve disease will cause AF. The protocol does not specify from where the imaging data are obtained and the manuscript reflects this. This is a ‘real world’ study, and we do not seek to add additional measures or processes unrelated to routine clinical care, other than those necessary to assess AF occurrence.

**Page 13, line 30: what about new anticoagulation medication, dabigatran, etc?**

We are grateful for the reviewer for pointing out this oversight. We have amended the manuscript from ‘warfarin’ to ‘anticoagulation’.

**Page 13, line 35: Could you elaborate on other adverse events associated with potassium administration? Arrhythmia's, or the line infections you mentioned earlier? Therefore, would you also collect data on duration of indwelling central lines?**

These are already fully described in the introduction. Data regarding the duration of indwelling central lines will not be collected as part of this feasibility study, but this thoughtful point will be considered for the future full study.

**Page 13, line 53: You did not provide some thought on potential dropout, exclusion from analysis, or loss to follow up from the 160 pilot patients. Do you estimate protocol violations will be exclusively 10% cross overs? Or could there also be other nonadherence? Could you please elaborate here what your strategy is? Do you for example enroll a certain percentage more than what is strictly needed?**

We thank the reviewer for pointing out that our manuscript limited itself to describing protocol violations in terms of cross-over. To clarify that there may be a number of causes of protocol violation, we have added the following statement below the primary endpoint section:

*“Reasons for a protocol violation may include:*

* *A patient from the ‘Relaxed’ group being treated as if they are in the ‘Tight’ Group, or a patient from the ‘Tight’ group being treated as if they are in the ‘Relaxed’ Group*
* *Failure of randomisation*
* *Alteration in planned surgery*
* *Failure of Holter monitoring process*
* *Lack of data completion”*

As requested, we have added the following statement to the statistical analysis section:

“*Due to this anticipated protocol violation rate, a greater number of patients will be recruited to the full study, as not all will be included in the final analysis.”*

**Page 14, line 15: please explain why you choose a one-sided alpha as opposed to two-sided.**

We apologies for the confusion surrounding the proposed sample size calculations for the main trial. We have edited the text to clarify that the proposed sample size is in fact 1682 and that the one sided alpha is 2.5% corresponding to a two sided alpha of 5%. The original figure of 1770 was 20% of the eligible (as targeted by our feasibility study) but we can see that this is misleading.

The formula used was

n = f(α, β) × [πs × (100 − πs) + πe × (100 − πe)] / (πs − πe − d)2

where πs and πe are the true percent 'success' in the standard and experimental treatment group respectively, and f(α, β) = [Φ-1(α) + Φ-1(β)]2

With regards to using a one sided alpha this is common practice with non-inferiority trials where interest is in one direction however we have clarified that it should have read a 2.5% one sided alpha and that this corresponds to the standard 5% two sided alpha.

**Page 15, line 34: please elaborate a bit on how you will store patient data. Is it on a certain server, behind firewalls? Will it be pass word protected? Who will have access? Will it be locked?**

We thank the reviewer for their query.

Electronic data will be stored in a fully audited data-centre in the UK with appropriate certifications including ISO 27001:2005 (Information Security) and 9001:2008 (Quality Management). The data will be mirrored to another server located elsewhere in the UK and backed up daily to tape. All connections to web applications will be accessed via encrypted HTTPS connections using industry-standard Transport Layer Security (TLS). Online applications will be secured through role permissions and individual password protection; audit trails will be maintained throughout. Any personal data on paper will be kept on site at the recruiting hospital. These will be stored in a locked office at each site compliant with GCP guidelines. Copies of paper data required by the Clinical Trials Unit will be faxed to a secure fax machine or scanned and sent as a password protected pdf. These copies will be stored in a locked filing cabinet in a locked room with restricted key card access compliant with GCP guidelines.

In response, the following text has been added to the Trial Governance section of the manuscript:

“*Electronic data will be stored in a fully audited data-centre in the UK with appropriate certifications including ISO 27001:2005 (Information Security) and 9001:2008 (Quality Management)*.”

**Page 18, line 33: Could you also discuss the potential limitation or potential selection bias that can be introduced by having potassium checked at the consulting physician's discretion? What I mean is that the consulting physician is not blinded as far as I know, so therefore, to check if his potassium strategy is effective in the tight control arm, he or she could order more frequent potassium lab tests in the tight control arm, versus the relaxed control arm. This could lead to potential undertreatment of the relaxed control arm, or overtreatment of the tight control arm.**

We are grateful to the Reviewer who makes a very good point regarding selection bias. This point is very applicable for the future full study but not for this feasibility study. The Protocol Development Group will carefully consider whether the number of potassium checks should be a secondary outcome measure for the future full study. We are doubtful that elaborating on this point will enhance this manuscript which describes the feasibility study.