Author’s response to reviews

Title: A single-centre, randomised controlled feasibility pilot trial comparing performance of direct laryngoscopy versus videolaryngoscopy for endotracheal intubation in surgical patients

Authors:

Alice Loughnan (a.loughnan@nhs.net)
Carolyn Deng (caro.deng@gmail.com)
Felicity Dominick (fliss_dom@hotmail.com)
Lora Pencheva (lioliu_nz@yahoo.com)
Douglas Campbell (d.campbell@adhb.govt.nz)

Version: 3 Date: 07 Mar 2019

Author’s response to reviews:

To the Editor

Re: A single-centre, randomised controlled feasibility pilot trial comparing performance of direct laryngoscopy versus videolaryngoscopy for endotracheal intubation in surgical patients

Thank you for your review of the above manuscript. We have highlighted the reviewer comments below and inserted a point by point comment of our own. Our comments are marked as responses.

Amendments in the manuscript can be seen as tracked changes

1. Page 5 line 26 and page 6 line 9, please define DL and VL on first use in main text (done in abstract but not main text).

Response: This has been altered see manuscript, see tracked changes
2. Please explain the rationale for the sample size more clearly (as per reviewer comment) - why choose 5% difference between techniques? Why is this not a non-inferiority trial? Is a difference to be expected between these two techniques?

Response: The sample size is not based on 5% differences between techniques. It is based upon a sample size sufficient to make a reliable estimate of the primary endpoint eg the confidence level method described in Thabane et al. The choice of +/- 5% for the estimate of proportion was arbitrary but was used to allow sufficiently accurate estimate of trial outcomes to make decisions for design of a larger trial. The method we have used conforms to best practice for sample size calculation for pilot trials (Thabane et al). Please see changes made to manuscript explaining this.

This is a pilot study where the primary aims are feasibility aims so a non-inferiority trial design is not appropriate. In the subsequent large trial we are designing, a non-inferiority design is one design we have considered. However, the primary scientific results from our pilot are somewhat counterintuitive in that traditional laryngoscopy appears to be superior. The prevailing published and clinical view is that VL will be superior. Our pilot results are evidence not in favour of a non-inferiority design for a subsequent large trial as there appears to be equipoise as to the superiority of VL or DL.

3. Page 9 were the assessors trained to be consistent in their outcome assessments? How?

Response: Yes. All outcome assessors went through a standardised training process prior to trial initiation. Primary endpoint definition was well defined and instruction as to how to adjudicate was provided. See tracked changes

4. Please add 95% confidence intervals are calculated to the statistical methods and add CIs to Table 5 (CIs are recommended rather than p-values in pilot trials).

Response: alterations made to manuscript, see tracked changes. CI added.

5. In Results (page 10) please add explanation for 6 missing outcomes - why? Please comment on results in Table 3 briefly in the text.

Response: changes to manuscript made, see tracked changes
6. In discussion please explain implications for pass rate <85% (besides sample size would be too large for main trial). Is this an expected pass rate? Is it usually lower? Give some justification for this choice.

Response: The prevailing clinical view is that first pass intubation success rates are high eg >90%. Our results show that this is not true in a clinical trial setting. In unexpected difficult intubation, repeated attempts are often necessary. If first-pass success rate is 90%, then subsequent attempts will have a proportionately lower success rate. Small differences in first-pass success rate may result in clinically important differences in overall intubation success after repeated attempts, avoid repeated airway trauma and reduce incidence of failed intubation. See tracked changes in manuscript detailing above justification.

7. Please also provide some discussion on why this should not be an equivalence or non-inferiority trial - this would be interesting for readers to see. Were you expecting clear superiority of one technique over the other?

Response: The choice to perform a non-inferiority trial is answered in 2. The primary hypothesis is clinically driven. A large trial will be an effectiveness trial so aims to change real world decision making. An equivalence trial would not provide evidence to change practice. Neither design is appropriate for a pilot trial. Both are designs that will be considered for a large trial, but at this stage a superiority trial is currently favoured for reasons explored in 2 and 7. Please see tracked changes to manuscript.

8. Page 12 line 39 this is not an effectiveness trial (that is what the main trial is for) - please replace the use of the word 'effectiveness' twice with a more appropriate word eg 'pilot trial' to determine potential harms.

Response: changes made to manuscript, see tracked changes.

Reviewer #3: Main body:

Sample size:

I really don't get what the authors want to say here 'we used a one sided 80% confidence interval
approach based on our feasibility objectives, which was an effect size of 5%, to estimate our required sample size. (18) (19) The effect size of 5% was based on binary outcomes of the incidence of first pass intubation success.'

Need more clarification. The authors can follow the guidelines how to write sample size section.

Response: The sample size is not based on 5% differences between techniques. It is based upon a sample size sufficient to make a reliable estimate of the primary endpoint eg the confidence level method described in Thabane et al. The choice of +- 5% for the estimate of proportion was arbitrary but was used to allow sufficiently accurate estimate of trial outcomes to make decisions for design of a larger trial. The method we have used conforms to best practice for sample size calculation for pilot trials (Thabane et al). Please see changes made to manuscript explaining this.

Statistical analysis:

It's not clear the types of outcomes. It's better to mention which method was used for which outcome- not general statement. Also, nothing mentioned what type of effect estimates were reported and whether confidence intervals were reported.

Response: reworded in manuscript to be more specific, please see tracked changes

Results:

In table 3, several IQRs were reported. Were these IQRs or Q1-Q3?

Response: These are Q1-Q3, changes have been made in manuscript and tables

Table 4, what does this mean 'Recruitment rate n=100'?

Response: number recruited, changes made in table to make this clearer

Figure 1, no reason for exclusion mentioned.

Response: reason for exclusion was due to missing data, this is detailed in figure 1
Results were reported for only two methods 'Pearson's Chi-squared test' and 'Wilcoxon Rank-sum (Mann-Whitney) test'. Why so many methods were mentioned in the statistical analysis section. Further, nothing was mentioned in the results section the results of checking normality, but it was mentioned in the statistical analysis section, why?

Response: methods section reworded, please see manuscript. It is not convention to report the results of tests of normality in the results section of a paper but it has been added in this instance.

Why no confidence interval was reported? It's better to report confidence intervals rather than p-values.

Response: CI added to text and tables

Discussion:

The authors said this was an effectiveness trial. I was wondering whether the authors know the difference between effectiveness, efficacy and pilot trial?

Response: Please see responses to editor and changes made in discussion section