PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (see an example) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below. Some articles will have been accepted based in part or entirely on reviews undertaken for other BMJ Group journals. These will be reproduced where possible.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Medication Intensification in diabetes in rural primary care: a cluster-randomized effectiveness trial.
AUTHORS	Estrada, Carlos; Billue, Katherine; Safford, Monika; Salanitro, Amanda; Houston, Thomas; Curry, William; Kim, Yongin; Allison, Jeroan

VERSION 1 - REVIEW

REVIEWER	Patrick J. O'Connor MD MA MPH Senior Clinical Investigator Co-Director Center for Chronic Care Innovation HealthPartners Research Foundation Minneapolis MN USA No conflicts of interest.
REVIEW RETURNED	05-Jun-2012

GENERAL COMMENTS	The auhtors report that a low-intensity mulit-component physician intervnetion using Web-based continuing medical education, performance feedback, and quality improvement tools did not improve medicaiton intensification for glucose, BP, or lipid control in adults with diabetes. These results suggest that other avenues fo care improvment, or else more intensive approaches than the one they executed, may be needed to achieve the stated goals and improve care. Interventiosn that (a) do not require a physician to trigger them (b) save physicians time, and (c) provide detialed clincial decision support for a complex clincial domain may be more effective. Alhtough this is a "negative" trial, the experiecnes reproted can help us all as we move forward and attempt new approaches to improve diabetes care. One such promising alternative approach is to provide point-of-care clincial decisison support via EMR tenchology (and Websites) in primary care settings.

REVIEWER	John F. Steiner Senior Director, Institute for Health Research Kaiser Permanente Colorado USA
REVIEW RETURNED	20-Jun-2012

THE STUDY	There is an inconsistency as to whether physicians or practices were the unit of randomization; more detail is requested about the measure of medication intensification, and all necessary documents are reported in the work itself.
GENERAL COMMENTS	This paper is a secondary analysis of an ambitious cluster-randomized trial to intensify diabetes treatment in rural primary care settings in the Southeastern US. Strengths of the original study (previously reported elsewhere) include: the cluster-randomized design; the Web-based intervention, which is particularly useful for studies of care in rural areas; the inclusion of multiple intervention components rather than a single intervention modality; and the willingness of the authors to publish a study showing that the overall intervention was not effective. When an effectiveness trial reaches a "null" conclusion, much can still be learned from careful analyses of the reasons for that outcome. This secondary analysis contributes by demonstrating that the intervention did not lead to treatment intensification, a precondition for improving risk factor control in diabetes. Some of the concerns about the current report are fundamentally concerns about the original trial. In specific: 1. There was a steep drop between the number of randomized units (205), and the number providing data (95). The reasons for that drop-off are described in Figure 1. However, Figure 1 suggests that practices were the unit of randomization, but this paper suggests that the unit of randomization was the physician. This discrepancy should be clarified – were these all solo practices? 2. While the need to balance rigor and cost of such a study was recognized, there is no explanation for the use of a serial, cross-sectional sample of patients rather than a second chart review for patients sampled at baseline. This approach may have reduced the power of the study to detect differences. 3. This and other such studies would benefit from a conceptual model that specifies how such an intervention might work if it is effective, and (by implication) what the main reasons for lack of effectiveness would be. A systematic "post-mortem" of a negative trial which assesses the reasons for the lack of intervention success could be very enlightening. The current paper looks at only one component of the process, namely treatment intensification. While this issue is thoroughly explored for all risk factors, readers would also be interested in a more comprehensive analysis of the multiple reasons for a null result. If some of those analyses were presented as part of other publications, it would be useful to summarize them in the discussion section of this paper. 4. The authors appropriately use RE-AIM as an evaluation framework, but again it would be instructive (consistent with point 3) to quantify each of the RE-AIM components. For example, it appears that reach was 205 practices agreeing out of 364 eligible = 56%. 5. It would be helpful to list all covariates that were adjusted for in the models; currently only examples are given. 6. Although it is not a big issue in an e-publication, the discussion of other RCTs in this area could be condensed substantially. It is helpful to cite the studies and briefly summarize their similarities and differences, but many of the detailed results of those other studies

	could be omitted here. 7. Several algorithms for calculating treatment intensification are now in use – a citation of the existing method used in this study (if any) would be helpful. If the authors are proposing a new method of assessing treatment intensification, it would be useful to compare the findings of their method to others in the literature (such as the method used in the O'Connor study).

REVIEWER	Tim Pickles, Statistician, South East Wales Trials Unit, Cardiff University, Wales, UK
REVIEW RETURNED	06-Jul-2012

GENERAL COMMENTS	Reviewer: Tim Pickles, Statistician, South East Wales Trials Unit, Cardiff University Quick summary: This cluster-randomized trial (The Rural Diabetes Online Care [R-DOC] study) compared patients of physicians randomized to access a medical education website (intervention arm) against patients of physicians randomized to access a limited version of the website (control arm). Following registration, inclusion and exclusion, recruitment, randomization and drop out, 95 physicians (48 intervention; 47 control) provided data on patients. The data was gleaned in such a way that that the baseline and follow-up formed two separate cross-sections of patients attending in the clinics of the partaking physicians. The main outcomes of this trial, measures of acceptable and optimal control for A1c, BP and LDL, have been previously reported and this paper hence reports a secondary outcome – medication intensification. The analysis (using GLMM in SAS) shows the intervention has no significant effect on this outcome. The bulk of this paper is very well written and is of high quality. The abstract contains all relevant information to get a grasp of this trial. The introduction states the problem, the parts of the trial already done and how this differs from the original in a clear and concise manner. The methods section covers lots of detail, including randomisation, inclusion/exclusion criteria, descriptions of the intervention in both arms, the sample size and data sources. The outcome is relevant for the question being asked and is very well defined, to the merit of the authors. The statistical analysis is well detailed and the authors are to be commended for the acknowledging the need to account for clustering here. The results section fully describes all the analysis as shown in the tables and figures. The discussion is well thought out, with limitations and implications of the trial, and a concise conclusion that does not over-exaggerate the overall findings of this trial. The references are relevant and up-to-date and, finally, the tables and figures add to the results section well and are presented excellently. However, despite the largely excellent work here, I have a number of comments, corrections and questions I would like to highlight here. Some of them may be personal preference but I hope none are trivial. I am going to refer to decimal places (dps) in the following as they are a particular bugbear of mine …

Abstract:

- The only comments I have here are mirrored in the results section, so if you make any changes there as a results of anything I have mentioned, please reflect them in the results within the abstract too.

Introduction:

- The p-value quoted as p=0.05 must be given to 3dps.

Methods:

- There is some missing information in Data Sources that is mentioned in reference 15 but not here. Intervention arm physicians provide 15 records at baseline BUT only 10 at follow-up. I spent a long time trying to figure out why Table 1 contained so many fewer intervention patients at follow-up compared to baseline;
- The 20% drop-out mentioned in reference 15 was not recognised – in fact it was almost 50%. There is no mention of this, or the implications of it, here or in reference 15. Whilst it may not be hugely pertinent here (what with this paper focussing on a secondary outcome), it might be worth mentioning this fact in the limitations;
- It is unusual for a before and after trial to report on two completely different cross-sections at the two time-points. The same patients before and then after is the way I have operated in similar trials. What you have done is fine and you have reported what you did correctly, but you could add why you did this;
- Whilst the statistical sections of both this paper and reference 15 mention accounting for clustering in the analysis, was there any notion of clustering/intra-cluster correlation coefficients/average cluster sizes in calculating the sample size?;
- Reference 29 is in brackets but should be superscripted;
- Remove the quote marks from around acceptable and optimal in Outcomes
- In Statistical Approach, there is no need for comparison between arms for baseline and follow-up characteristics. The purpose of reporting these is to show any imbalances, which can be seen by eye, without need for statistical testing;
- In Statistical Approach, you say that the study wasn't powered to look at medication intensification stratified by level of control. Surely, though, it wasn't powered to look at medication intensification at all, but to look at the primary outcome dealt with in reference 15;
- In Statistical Approach, you mention conducting a per-protocol analysis of web engagement. Where is this analysis?

Results:

- In Recruitment Scheme, Patient Characteristics and Web Utilization, the number 95, 1182 and 945 should be split by arm, as well as given in total. Also, the word Ninety in the last sentence should be replaced by 90 and both that and the given percentage should be split by arm, as well as bring given in total;
- p-values must be reported as p=0.xxx (3dps) or p<0.001. That is a lower case p, not upper case;
- In Main Outcome - Medication Intensification, there is a space (or underscore) before the title;
- In Main Outcome - Medication Intensification, the first

	paragraph contains all the required information but the next two miss out the percentages. Can they be added for completeness?; • In Main Outcome - Medication Intensification, a lower bound of a 95% CI is quoted as 0.7. Can this be given to 2dps?; • In Main Outcome - Medication Intensification, the last paragraph is actually the main result of the trial, so why does it not come first?; • In Secondary Outcome - Medication Intensification by Strata, you give a lot of attention to A1c results but not to BP or LDL results. Granted they are not significant like some of the A1c results but it depends on what you are looking at. The only comparisons made here are from baseline to follow-up within strata within arm within medication type. Why not compare baseline to follow-up across strata or baseline to follow-up in the same strata across arm? For instance, for LDL >=130mg/dL, a comparison of baseline to follow-up between arms would most likely be significant. Discussion: • Nothing. References: • References 18 and 19 point to the same spot in the same academic journal. Something needs changing here. Tables and Figures: • In Table 1, there is no need for p-values. See earlier point made in Methods. These columns could show the totals instead; • The SDs for age should have 2dps; • The percentages should all have 1dp; • For Depression at follow-up, the percentage for Control is prefixed by a 9. It should be an open bracket; • In the footnotes of Table 1, the definition of obesity should include units for body mass index • In Figure 1, the word practices is used throughout but the text largely uses physicians or just participants. For the sake of consistency, I think it may be sensible to change the wording in the Figure; • In Figures 2 and 3, all p-values required 3dps and a lower case p CONSORT check list: • In both cases where stated 'could request permission to reproduce' etc …, I would create modified versions here • You state that the protocol can be accessed and is available on page 4. None of the references on page 4 (that's 13 and 15 to 19) are the study protocol. Page 4 mentions the protocol was approved but this is not the same. Therefore, put N/A for this as it is not available

VERSION 1 – AUTHOR RESPONSE

Reviewer: Patrick J. O'Connor MD MA MPH

Senior Clinical Investigator

Co-Director

Center for Chronic Care Innovation

HealthPartners Research Foundation

Minneapolis MN USA

No conflicts of interest.

The auhtors report that a low-intensity mulit-component physician intervnetion using Web-based continuing medical education, performance feedback, and quality improvement tools did not improve medicaiton intensification for glucose, BP, or lipid control in adults with diabetes.

These results suggest that other avenues fo care improvment, or else more intensive approaches than the one they executed, may be needed to achieve the stated goals and improve care. Interventiosn that (a) do not require a physician to trigger them (b) save physicians time, and (c) provide detialed clincial decision support for a complex clincial domain may be more effective.

Alhtough this is a "negative" trial, the experiecnes reproted can help us all as we move forward and attempt new approaches to improve diabetes care. One such promising alternative approach is to provide point-of-care clincial decisison support via EMR tenchology (and Websites) in primary care settings.

Reviewer: John F. Steiner

Senior Director, Institute for Health Research

Kaiser Permanente Colorado

USA

as noted in comments to author - there is an inconsistency as to whether physicians or practices were the unit of randomization; more detail is requested about the measure of medication intensification, and all necessary documents are reported in the work itself.

AU Response: We appreciate the comment and have addressed all comments, see below.

This paper is a secondary analysis of an ambitious cluster-randomized trial to intensify diabetes treatment in rural primary care settings in the Southeastern US. Strengths of the original study (previously reported elsewhere) include: the cluster-randomized design; the Web-based intervention, which is particularly useful for studies of care in rural areas; the inclusion of multiple intervention components rather than a single intervention modality; and the willingness of the authors to publish a study showing that the overall intervention was not effective. When an effectiveness trial reaches a "null" conclusion, much can still be learned from careful analyses of the reasons for that outcome. This secondary analysis contributes by demonstrating that the intervention did not lead to treatment intensification, a precondition for improving risk factor control in diabetes.

Some of the concerns about the current report are fundamentally concerns about the original trial.

In specific:

1. There was a steep drop between the number of randomized units (205), and the number providing data (95). The reasons for that drop-off are described in Figure 1. However, Figure 1 suggests that practices were the unit of randomization, but this paper suggests that the unit of randomization was the physician. This discrepancy should be clarified – were these all solo practices?
   AU Reponse: The unit of randomization was the physician (and not a practice); however, for physicians working in a group practice, only one physician per practice could enroll in the study. We have added this wording in the Methods section (under Study Design and Setting).

   We have also modified the following wording of the first paragraph in the Data Sources description in the Methods section: "All participating physicians provided copies of records of 15 (intervention arm physicians) or 10 (control arm physicians) *of their own* consecutively seen patients with diabetes at baseline and again at follow up (representing two cross-sectional views of *each physician's panel of patients*)."

   We have also added 2 references explaining the need for a larger size for feedback purposes, references #19 and #20:

   19. Allison JJ, Calhoun JW, Wall TC, Spettell CM, Fargason Jr CA, Weissman NW, et al. Optimal reporting of health care process measures: inferential statistics as help or hindrance? Manag Care Q 2000;8(4):1-10.

   20. Holmboe ES, Meehan TP, Lynn L, Doyle P, Sherwin T, Duffy FD. Promoting physicians' self-assessment and quality improvement: the ABIM diabetes practice improvement module. J Contin Educ Health Prof 2006;26(2):109-19.

   Finally, we reviewed the text for internal consistency (practice vs. own patients) and made changes in the CONSORT diagram.

2. While the need to balance rigor and cost of such a study was recognized, there is no explanation for the use of a serial, cross-sectional sample of patients rather than a second chart review for patients sampled at baseline. This approach may have reduced the power of the study to detect differences.
   AU Response: The reviewer points out an important feature of our design. We have added the following wording under Data sources, Methods section: "Since the focus of the intervention was the physician, we were less interested in specific patients but rather each physician's panel on average. Therefore, 2 samples as serial cross

sections would better represent any change in the physician's own panel on average. This method is similar to practice feedback for quality improvement purposes."

3. This and other such studies would benefit from a conceptual model that specifies how such an intervention might work if it is effective, and (by implication) what the main reasons for lack of effectiveness would be. A systematic "post-mortem" of a negative trial which assesses the reasons for the lack of intervention success could be very enlightening. The current paper looks at only one component of the process, namely treatment intensification. While this issue is thoroughly explored for all risk factors, readers would also be interested in a more comprehensive analysis of the multiple reasons for a null result. If some of those analyses were presented as part of other publications, it would be useful to summarize them in the discussion section of this paper.

   AU response: Thanks for the comment, we certainly agree on the importance of studying the study itself, and the mechanistic explanations for the results (whether positive or negative). We attempted to obtain measures of how busy the clinicians were at the end of trial; however, the very low response rendered the results completely uninformative. We chose not to include this information. Added in text, Discussion section, last portion of Limitations: "Although a comprehensive analysis would have been enlightening, we did not perform a systematic examination of this negative trial, or how such intervention might work it were effective. We worried that studying the study while being conducted would have introduced another variable."

4. The authors appropriately use RE-AIM as an evaluation framework, but again it would be instructive (consistent with point 3) to quantify each of the RE-AIM components. For example, it appears that reach was 205 practices agreeing out of 364 eligible = 56%. **AU response: See response above. While we based our intervention in the RE-AIM framework, the measurement of all components of this framework was outside the scope of the study.**

5. It would be helpful to list all covariates that were adjusted for in the models; currently only examples are given. **AU response: We appreciate the comment, all covariates were included in the description of the Statistical approach in the Methods section. Adjusted for race and clinical diagnosis of hypertension or depression.**

6. Although it is not a big issue in an e-publication, the discussion of other RCTs in this area could be condensed substantially. It is helpful to cite the studies and briefly summarize their similarities and differences, but many of the detailed results of those other studies could be omitted here. **AU response: We appreciate the comment. We have condensed this section as requested and maintained the key design and results features for comparative purposes. As the interventions and measures of the studies were very different than ours, we maintained the description of similarities and differences within each section.**

7. Several algorithms for calculating treatment intensification are now in use – a citation of the existing method used in this study (if any) would be helpful. If the authors are proposing a new method of assessing treatment intensification, it would be useful to compare the findings of their method to others in the literature (such as the method used in the O'Connor study).

AU response: **The reviewer poses an important comment. Medication intensification is an area of study. No agreed upon recommendation exists on a uniform recommendation. At the time of study design and registration (Trial registration: NCT00403091) in 2006, few definitions were available. The O'Connor study was published at a later time and we are not proposing a new method of assessment treatment intensification (this would have required the analysis of several ways to measure an compare methodologies). While important, comparing methods was beyond the study design and objectives.**

Reviewer: Tim Pickles, Statistician, South East Wales Trials Unit, Cardiff University, Wales, UK

Quick summary:

This cluster-randomized trial (The Rural Diabetes Online Care [R-DOC] study) compared patients of physicians randomized to access a medical education website (intervention arm) against patients of physicians randomized to access a limited version of the website (control arm). Following registration, inclusion and exclusion, recruitment, randomization and drop out, 95 physicians (48 intervention; 47 control) provided data on patients. The data was gleaned in such a way that that the baseline and follow-up formed two separate cross-sections of patients attending in the clinics of the partaking physicians. The main outcomes of this trial, measures of acceptable and optimal control for A1c, BP and LDL, have been previously reported and this paper hence reports a secondary outcome – medication intensification. The analysis (using GLMM in SAS) shows the intervention has no significant effect on this outcome.

The bulk of this paper is very well written and is of high quality. The abstract contains all relevant information to get a grasp of this trial. The introduction states the problem, the parts of the trial already done and how this differs from the original in a clear and concise manner. The methods section covers lots of detail, including randomisation, inclusion/exclusion criteria, descriptions of the intervention in both arms, the sample size and data sources. The outcome is relevant for the question being asked and is very well defined, to the merit of the authors. The statistical analysis is well detailed and the authors are to be commended for the acknowledging the need to account for clustering here. The results section fully describes all the analysis as shown in the tables and figures. The discussion is well thought out, with limitations and implications of the trial, and a concise conclusion that does not over-exaggerate the overall findings of this trial. The references are relevant and up-to-date and, finally, the tables and figures add to the results section well and are presented excellently.

However, despite the largely excellent work here, I have a number of comments, corrections and questions I would like to highlight here. Some of them may be personal preference but I hope none are trivial. I am going to refer to decimal places (dps) in the following as they are a particular bugbear of mine.

AU response: **We have changed to the required decimal places throughout the manuscript (except in the Introduction as it quotes a published study).**

Abstract:

- The only comments I have here are mirrored in the results section, so if you make any changes there as a results of anything I have mentioned, please reflect them in the results within the abstract too. **AU response: We have reviewed the manuscript for internal consistency with the Abstract.**

Introduction:

- The p-value quoted as p=0.05 must be given to 3dps. **AU response: The p value in the Introduction was obtained from a published study, the published study only displayed 2dps. No change made.**

Methods:

- There is some missing information in Data Sources that is mentioned in reference 15 but not here. Intervention arm physicians provide 15 records at baseline BUT only 10 at follow-up. I spent a long time trying to figure out why Table 1 contained so many fewer intervention patients at follow-up compared to baseline; **AU response: See response above, item #1, page 5 (Reviewer: John F. Steiner).**

- The 20% drop-out mentioned in reference 15 was not recognised – in fact it was almost 50%. There is no mention of this, or the implications of it, here or in reference 15. Whilst it may not be hugely pertinent here (what with this paper focussing on a secondary outcome), it might be worth mentioning this fact in the limitations; **AU Response: We now emphasize more the attrition in the Limitations section of the Discussion as suggested. Added: "Second, the high attrition, *95 of the 205 randomized physicians provided baseline and follow-up data,* may have introduced biases."**

- It is unusual for a before and after trial to report on two completely different cross-sections at the two time-points. The same patients before and then after is the way I have operated in similar trials. What you have done is fine and you have reported what you did correctly, but you could add why you did this;

AU Response: Same response as above (Reviewer: John F. Steiner). The reviewer points out an important feature of our design. We have added the following wording under Data sources, Methods section: "Since the focus of the intervention was the physician, we were less interested in specific patients but rather each physician's panel on average. Therefore, 2 samples as serial cross sections would better represent any change in the physician's own panel on average. This method is similar to practice feedback for quality improvement purposes."

- Whilst the statistical sections of both this paper and reference 15 mention accounting for clustering in the analysis, was there any notion of clustering/intra-cluster correlation coefficients/average cluster sizes in calculating the sample size?;

AU response: **As requested by another reviewer, we now include the sample size estimates from the original publication for the primary outcomes (A1c, blood pressure, and LDL control). We acknowledge that the power may not have been sufficient to detect such differences, given the attrition we observed poses a limitation to our findings (included in the Limitations section of the Discussion).**

- Reference 29 is in brackets but should be superscripted; **AU response:** **Thanks for noticing, this was a typographical error. Changed to reference 15.**

- Remove the quote marks from around acceptable and optimal in Outcomes. **AU response:** **Change as suggested made.**

- In Statistical Approach, there is no need for comparison between arms for baseline and follow-up characteristics. The purpose of reporting these is to show any imbalances, which can be seen by eye, without need for statistical testing; **AU response:** **Thanks. We have now removed the p values.**

- In Statistical Approach, you say that the study wasn't powered to look at medication intensification stratified by level of control. Surely, though, it wasn't powered to look at medication intensification at all, but to look at the primary outcome dealt with in reference 15; **AU response:** **As requested above, we have included the sample size calculations for the original study.**

- In Statistical Approach, you mention conducting a per-protocol analysis of web engagement. Where is this analysis? **AU response:** **The sentence was included in error in this manuscript, the per-protocol analysis was done in the main results manuscript. We have removed such wording.**

Results:

- In Recruitment Scheme, Patient Characteristics and Web Utilization, the number 95, 1182 and 945 should be split by arm, as well as given in total. Also, the word Ninety in the last sentence should be replaced by 90 and both that and the given percentage should be split by arm, as well as bring given in total;

AU response: **We have now included the information requested and matches the information from the CONSORT diagram and Table 1.**

Ninety. We have reworded the sentence: "Of the 95 physicians, 90 (94.7%) had access to the Internet in the office."

- p-values must be reported as p=0.xxx (3dps) or p<0.001. That is a lower case p, not upper case; **AU response: P values were changed to 3dps and lower case throughout the manuscript, table, and figures.**

- In Main Outcome - Medication Intensification, there is a space (or underscore) before the title; **AU response: Removed.**

- In Main Outcome - Medication Intensification, the first paragraph contains all the required information but the next two miss out the percentages. Can they be added for completeness?; **AU response: Thanks, now the percentages are included.**

- In Main Outcome - Medication Intensification, a lower bound of a 95% CI is quoted as 0.7. Can this be given to 2dps?; **AU response: Thanks, this was our typographical error. It now reads 0.72.**

- In Main Outcome - Medication Intensification, the last paragraph is actually the main result of the trial, so why does it not come first?; **AU response: We appreciate the comment, we have now moved it to the first portion of the paragraph. Also, upon reviewing the statistical output files to provide the 3 decimal points, we identified a typographical error which has been corrected (correct p value = 0.948; prior p value = 0.82).**

- In Secondary Outcome - Medication Intensification by Strata, you give a lot of attention to A1c results but not to BP or LDL results. Granted they are not significant like some of the A1c results but it depends on what you are looking at. The only comparisons made here are from baseline to follow-up within strata within arm within medication type. Why not compare baseline to follow-up across strata or baseline to follow-up in the same strata across arm? For instance, for LDL >=130mg/dL, a comparison of baseline to follow-up between arms would most likely be significant. **AU response: We appreciate the thoughtful comment. We spent more space on medications to improve glucose management, as this was the main group of medications for patients with diabetes (it does apply to all patients once the diagnosis is established). The less emphasis for hypertensions and hyperlipidemia is that only a fraction of patients with diabetes would have abnormal values. The number of patients who comprised these groups was small, rendering the adjusted analysis unstable; the PROC GLIMMIX resulted in a non-convergence error when we attempted this approach. Finally, we hope that the reader has the same visual impression for future studies. Taken collectively, expanding on this area would seem to distract from the other aspects of the results. No further changes made.**

Discussion:

- Nothing.

References:

- References 18 and 19 point to the same spot in the same academic journal. Something needs changing here. **AU response: We appreciate the reviewer's noticing this error. Corrected now (only one reference applies).**

Tables and Figures:

- In Table 1, there is no need for p-values. See earlier point made in Methods. These columns could show the totals instead; **AU response: We removed the p values and have added the total values as suggested.**

- The SDs for age should have 2dps; **AU response: Thanks, changed.**

- The percentages should all have 1dp; **AU response: Thanks, changed (and corrected a couple of typographical errors).**

- For Depression at follow-up, the percentage for Control is prefixed by a 9. It should be an open bracket; **AU response: The typographical error was corrected.**

- In the footnotes of Table 1, the definition of obesity should include units for body mass index. **AU response: Added.**

- In Figure 1, the word practices is used throughout but the text largely uses physicians or just participants. For the sake of consistency, I think it may be sensible to change the wording in the Figure; **AU response: Wording in the figure was changed and simplified as suggested.**

- In Figures 2 and 3, all p-values required 3dps and a lower case p. **AU response: We have now changed all p values with 3dps and lower case p.**

CONSORT check list:

- In both cases where stated 'could request permission to reproduce' etc …, I would create modified versions here. **AU response: See response to Editor above. IJQSHC requires permission to reproduce for information published. We will seek permission to reproduce the modified version after Editors review this submission (we acknowledge that other suggestions may emerge).**

- You state that the protocol can be accessed and is available on page 4. None of the references on page 4 (that's 13 and 15 to 19) are the study protocol. Page 4 mentions the protocol was approved

but this is not the same. Therefore, put N/A for this as it is not available.**AU response: A single publication of a study protocol per se, as is sometimes seen in other studies, is not available for the RDOC study. The wording included in Study Design and Setting was meant to provide the reader with additional detail from this study that has been expanded in other publications, modified to read: "Further details of the study design, web-content, recruitment and retention processes, and patient characteristics have been published elsewhere**

Would you be willing to share your data? Cast your vote in our <a href="http://80911.polldaddy.com/s/would-you-be-willing-to-share-your-data-in-an-open-repository"> Online Poll. **AU response: We decline.**

VERSION 2 – REVIEW

REVIEWER	Pickles, Timothy Cardiff University, South East Wales Trials Unit (SEWTU)
REVIEW RETURNED	15-Aug-2012

GENERAL COMMENTS	The authors have duly responded to the previous set of comments and the paper reads and feels much better. However, I state a few outstanding points below that need to be addressed before I am willing to 'Accept' this paper. Throughout • Picky perhaps but can you pick whether you want spaces one, both, or neither side of an equals sign? It just look messy when it is different all over the place Abstract, Secondary Outcomes – Medication Intensification by Strata and Figure 3 • Provide 1dp for all percentages on Figure 3, and then copy those percentages to where they are reported in the Abstract and in Secondary Outcomes – Medication Intensification by Strata Statistical Approach • Correctly removed p-values in Table 1 regarding baseline comparison but the wording "Patient characteristics were compared …" needs removing too • I don't see the reason for the addition of the new sentence "Although the age difference between intervention and control …" being added. The analysis is now not tabulated (correctly) and you specify that covariates included adjust for differences from baseline to follow-up, not intervention vs. control at baseline. The addition doesn't appear to be in relation to any comment, so can it be removed please. Recruitment Scheme, Patient Characteristics and Web Utilization • I can't fathom why the number for intervention patients at follow-up is 479. It may be correct but as I read it, intervention physicians should have 15 at baseline and follow-up, and control physicians should have 10 at baseline

	and follow-up. So shouldn't this 479 be up toward the 720 mark? Main Outcome - Medication Intensification • Why is the final paragraph laid out differently to the preceding two? It makes it difficult to read and isn't consistent Table 1 • Follow-up Control percentage for Hyperlipidemia has 2dps rather than 1dp

VERSION 2 – AUTHOR RESPONSE

Reviewer: Timothy Pickles

The authors have duly responded to the previous set of comments and the paper reads and feels much better. However, I state a few outstanding points below that need to be addressed before I am willing to 'Accept' this paper.

Throughout

• Picky perhaps but can you pick whether you want spaces one, both, or neither side of an equals sign? It just look messy when it is different all over the place. **AU RESPONSE: We have now changed all to no spaces before and after the equal sign throughout.**

Abstract, Secondary Outcomes – Medication Intensification by Strata and Figure 3

• Provide 1dp for all percentages on Figure 3, and then copy those percentages to where they are reported in the Abstract and in Secondary Outcomes – Medication Intensification by Strata

AU RESPONSE: We have now included the 1dp in Figure 3, Abstract, and Results (secondary outcomes).

Statistical Approach

• Correctly removed p-values in Table 1 regarding baseline comparison but the wording "Patient characteristics were compared …" needs removing too **AU RESPONSE: Thanks, we have now removed the sentence.**

• I don't see the reason for the addition of the new sentence "Although the age difference between intervention and control …" being added. The analysis is now not tabulated (correctly) and you specify that covariates included adjust for differences from baseline to follow-up, not intervention vs. control at baseline. The addition doesn't appear to be in relation to any comment, so can it be removed please. **AU RESPONSE: Sentence has been removed.**

Recruitment Scheme, Patient Characteristics and Web Utilization

• I can't fathom why the number for intervention patients at follow-up is 479. It may be correct but as I read it, intervention physicians should have 15 at baseline and follow-up, and control physicians should have 10 at baseline and follow-up. So shouldn't this 479 be up toward the 720 mark?

AU RESPONSE: Thanks for the comment. Intervention physicians provided 15 patients at baseline and 10 patients at follow-up. Control physicians provided 10 patients at baseline and 10 patients at follow-up. The first paragraph in the Statistical section has been reworded, it now reads:

> ***Statistical Approach***
> ***We calculated …… (10 patients per physician at baseline and at follow-up)*** [15]***. However, intervention arm physicians were asked to provide 15 patient records at baseline (and***

not at follow-up) because of the need to construct audit and feedback reports as part of the intervention [19 20] for A1c, BP…

Main Outcome - Medication Intensification

• Why is the final paragraph laid out differently to the preceding two? It makes it difficult to read and isn't consistent **AU RESPONSE: We have now changed the paragraph to match the preceding two. It now reads:**

In the unadjusted analysis, intensification of medications to control LDL did not differ for patients cared for by physicians in either trial arm when comparing baseline and follow up data (intervention, 10.6% vs. 11.3%, p=0.726; control, 8.1% vs. 8.4%, p=0.898 (Figure 2). This finding was consistent with the adjusted analysis (intervention, AOR 1.05 [95% CI 0.73, 1.50]; control, AOR 1.00, [95% CI 0.65, 1.53]).

Table 1

• Follow-up Control percentage for Hyperlipidemia has 2dps rather than 1dp. **AU RESPONSE: Corrected to 1dp.**