PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	The use of a patient centred educational exchange (PCEE) to improve patient's self-management of medicines after a stroke; a randomised controlled trial study protocol.
AUTHORS	Coombes, Judith; Rowett, Debra; Whitty, Jennifer; Cottrell, Neil

VERSION 1 – REVIEW

REVIEWER	Sheeba Rosewilliam University of Birmingham, UK.
REVIEW RETURNED	22-May-2018

GENERAL COMMENTS	The strengths and limitations can be rewritten to make them more specific to the current study rather than giving generic information (first two bullet points). The logical flow will be better if there is information about why adherence is reduced and how education fits in this context. It is good to mention theories of behaviour change underpinning the 'educational visiting' strategy; however, how the constructs from these theories are applied within this strategy is not clear. Hence naming the theories just makes this strategy appear complex. Perhaps a simple explanation of the educational visiting strategy would be more helpful for the readers to follow, than mention theories without elaboration. The level of communication for patients to be included in this study needs to be made clear since aphasias could impede delivery of intervention. PPI section needs proof reading. There is a random question mark within text here. Feasibility of acceptance from patients' viewpoint is clear, however, feasibility of application of intervention regarding time, resources and staff opinions (perhaps because it is the researcher who is delivering intervention) are not explicit in the results section for the feasibility study. But this should be acknowledged in limitations. Period when study will be carried out needs to be mentioned. Please include date and version for protocol.

REVIEWER	Paul Amuna Primary Health Care Corporation, Qatar
REVIEW RETURNED	31-May-2018

GENERAL COMMENTS	I have reviewed this manuscript and confirm that it is a non-blinded randomised controlled trial as stated by the authors. One group receives structured education (2 sessions). Control group gets only usual care. Follow up over 12 months.

	The authors have adhered to the SPIRIT criteria for clinical trials. **Introduction** Overall the language is excellent. The introduction is very well written and succinct with relevant and appropriately cited references cited in the text using the Vancouver style. The aims are clearly stated and are sound and logical. The investigators recognise the potential strengths and limitations of the study. **Study design.** This is well structured and detailed. I suggest the setting be presented as a stand-alone heading. The inclusion and exclusion criteria are clearly stated and appear justified to me e.g. using the Documented Mental State Questionnaire score 10/10 for inclusion and the assurance that those who are excluded will not be disadvantaged by not taking part. Patient and public involvement. This has been considered by the authors and although patients were not involved in the study design, there was a pre-testing of the research tools and patients were asked their opinions about tool once it was developed. Plans for recruitment are well stated and the process of randomisation described in sufficient detail. The authors have indicated their approach to concealment to avoid allocation bias. Allocation will be based on a random computer generated allocation four block code. They also acknowledge the fact that the investigator will no longer be blinded to the participant after allocation.

	The sample size, sample size calculation and considerations for loss to follow up have been well described. I am satisfied with the level of statistical input into the recruitment and sampling process. The approach used is both appropriate and justified in my opinion. The intended procedures are clearly described. I am satisfied that the control group will receive "Usual care" which is in itself well structured. The sessions for the intervention group are well outlined including a detailed description of the steps involved in the interview process. The hypothesis presented by the investigators that "patients in the intervention group will be influenced to organize their medication better than control group" is fair to me. Outcome measures include adherence to antithrombotic, antihypertensive and lipid lowering drugs as a measure of prevention of secondary stroke. Refill data will be used, self-reported medication taking behaviour, self-reported clinical outcomes, QOL, cost utility of using the medications, changes in beliefs towards stroke medication. Primary and secondary outcome measures are presented in logical manner and cover quite a wide range. This appears ambitious yet are realistic in my view although the investigators do not indicate how they will test economic outcomes statistically in sufficient detail. The data management section is generally well presented. The suggested methods of data collection, collation and analysis are sound. The investigators recognise that the large bulk of their data for the primary outcomes especially will be non-parametric and have rightly chosen an appropriate non-parametric statistical test (Mann-Whitney U test) **Ethical considerations** The investigators have provided a full explanation of the ethical issues relating to the project. They have provided information in lay language which covers issues of consent, privacy and respect of persons. They also assure participants of their autonomy and highlight the voluntary nature of the study and their freedom to withdraw from the study at any time they so wish. I am satisfied that the relevant ethical issues have been sufficiently addressed. **My only question relates to the matter of justice especially for those who because of their stroke may have difficulty communicating e.g. difficulty with speech and physical impairment. Although they will be excluded, they will**

	nonetheless receive adequate care without incurring any disadvantages. The authors have also set up a Data safety Management Committee to handle adverse events reporting and quality assurance. The trial is already registered with the Australian Clinical Trials registry. Issues of conflict of interest have also been addressed including trial sponsorship and funding. References are well cited and up to date. Appendix. I have examined the tools and other accompanying documents and find them satisfactory. I am satisfied that the investigators have presented a well designed study. I recommend its acceptance for publication.

VERSION 1 – AUTHOR RESPONSE

I have addressed the comments as below. I have also attached this as a file in table form.
Reviewer 1 Thank-you for your helpful review.
Reviewer-The strengths and limitations can be rewritten to make them more specific to the current study rather than giving generic information (first two bullet points).
Response- The first two bullet points have been rewritten.
• The design of randomising participants to the PCEE will give the opportunity to account for other changes across the time of the study.
• The use of questionnaires, validated as research tools, to elicit patient perceptions will be integrated with the approach used in “academic detailing”.

Reviewer-The logical flow will be better if there is information about why adherence is reduced and how education fits in this context.
Response-The following has been added to the end of the first paragraph- Reports of patient adherence to secondary prevention medications vary widely ranging from 40% to 86% and are influenced by the timing and method of measurement. There are many reasons reported for reduction in adherence including lower income, multiple co-morbidities, minor stroke or TIA, forgetfulness, trivialising stroke and low necessity beliefs in taking medications.
The first sentence of the second paragraph has been modified to read- Educational interventions focused on improving patient use of medications for secondary prevention of stroke have shown impact on patients’ knowledge but other outcome measures have had varied results.

Reviewer-It is good to mention theories of behaviour change underpinning the 'educational visiting' strategy; however, how the constructs from these theories are applied within this strategy is not clear. Hence naming the theories just makes this strategy appear complex. Perhaps a simple explanation of

the educational visiting strategy would be more helpful for the readers to follow, than mention theories without elaboration.
Response-Thank-you, I have removed the underpinning theories. I have added the key features of academic detailing, adapted from those described by Soumerai and Avorn in their 1990 paper, in the second paragraph of the introduction as follows. Academic detailing uses a social marketing framework, to encourage information exchange while delivering key messages in order to influence behaviour. The approach includes the following key features: identifying baseline knowledge and motivations for medication use, defining clear educational and behavioural objectives, establishing credibility, referring to authoritative sources of information, and presenting both sides of controversial issues, stimulating participation in educational interactions, using concise graphic educational materials, highlighting and repeating the essential messages and providing positive reinforcement of improved practices in follow-up communication.

Reviewer-The level of communication for patients to be included in this study needs to be made clear since aphasias could impede delivery of intervention.
Response-Thank-you, In the inclusion criteria it says the participant must " have a documented Mental Status Questionnaire (MSQ) score of 10/10 at the time of recruitment and be able to provide consent." The consent form also requires the researcher to sign the declaration which says. "I have given a verbal explanation of the research project, its procedures and risks and I believe that the participant has understood that explanation." This means the participant is unlikely to be aphasic or even have severe receptive or expressive dysphasia. It is possible that the participant may have a mild dysphasia.
I have added the following words to the inclusion criteria. The consent form requires the researcher to sign a declaration saying that they have given a verbal explanation of the research project, its procedures and risks and believe that the participant has understood that explanation. This means the participant is unlikely to have severe problems with verbal communication.

Reviewer- PPI section needs proof reading. There is a random question mark within text here.
Response-Thank-you. The PPI has been proof read with grammatical changes and the question mark has been removed.

Reviewer-Feasibility of acceptance from patients' viewpoint is clear, however, feasibility of application of intervention regarding time, resources and staff opinions (perhaps because it is the researcher who is delivering intervention) are not explicit in the results section for the feasibility study. But this should be acknowledged in limitations.
Response-Thank-you, As pointed out by the reviewer this is a researcher delivered intervention. I have added the following to paragraph 3 of the introduction. A limitation of this feasibility study was that because the researcher delivered the intervention, the training requirements, use of resources and opinions of staff were not evaluated.
Reviewer-Period when study will be carried out needs to be mentioned
Response-The first participant was consented on the 19/12/2015, and the study is ongoing until April 2019. The following has been added to the end of the recruitment section in the methods. The first participant was consented on the 19/12/2015, and the study is ongoing until April 2019.

Reviewer-Please include date and version for protocol.
Response- Protocol v1.3 dated 7/8/2015 was approved by Metro South Ethics on 29/9/2015. I have checked the date and version of the most recent amendment of the protocol and ensured this is correct in the footer of the protocol and the Patient information and Consent Form. This is the attached Protocol v2 17/02/16

Reviewer 2 Thank-you for your review.

Reviewer- I suggest the setting be presented as a stand-alone heading.
Response-Setting, is now a stand-alone heading see page 7

Reviewer-My only question relates to the matter of justice especially for those who because of their stroke may have difficulty communicating e.g. difficulty with speech and physical impairment. Although they will be excluded, they will nonetheless receive adequate care without incurring any disadvantages.
Response-In the study hospital patients with speech and physical impairment are referred for further rehabilitation which includes the provision of weekly education sessions as described in the first sentence of the exclusion criteria. I have added the following sentence to the end of the exclusion criteria, page 8. Those who are excluded will receive standard care, which includes education, without incurring any disadvantage.