PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Would primary health care professionals prescribe a polypill to manage cardiovascular risk? A qualitative interview study
AUTHORS	Greenfield, Sheila; Virdee, Satnam; Fletcher, Kate; McManus, Richard; Hobbs, Richard; Mant, Jonathan

VERSION 1 - REVIEW

REVIEWER	Vanessa Selak Senior Research Fellow National Institute of Health Innovation, University of Auckland, New Zelaand Competing interests: - Investigator on trial comparing polypill-based care with usual care in patients at high risk (IMPACT) - Dr Reddy's Laboratories Ltd provided their polypill (Red Heart Pill) free of charge for IMPACT trial - Received travel assistance from Dr Reddy's Laboratories Ltd to attend meetings on the polypill
REVIEW RETURNED	23-Dec-2012

THE STUDY	As indicated by authors, their sample of primary health care professionals was not representative. Statistical methods were not used, appropriately, as this research used a qualitative description approach. Additional references that would add weight to the paper are: - CTT collaboration. Effects of lowering LDL in people at low risk of disease. Lancet 2012 - Law et al. use of BP lowering drugs in the prevention of cardiovascular disease. BMJ 2009 - Yusuf et al. PURE study. Lancet 2011 - Elley et al. Efficacy and tolerability of 'polypills': a meta-analysis of RCTs. PLOS one 2012 (I am a co-author on this paper) Supplementary documents - none that I was able to access
REPORTING & ETHICS	No relevant reporting statement or checklist for this type of research that I am aware of. Authors should mention whether ethical consent was obtained to undertake the research and whether participants provided written informed consent to the research (and if not, why not). Table 1 should present collated, rather than individual participant, data.
GENERAL COMMENTS	This was a useful paper that has obtained the views of GPs and primary care nurses on the use of the polypill, primarily as envisaged by Wald & Law. It should be noted in the paper that in addition to blood pressure and lipid lower medication, Wald & Law proposed the addition of aspirin and folate in their polypill (as it was this combination that was used as the basis of the 80%+ reduction in CVD).

REVIEWER	Curt D. Furberg, MD, PhD Professor of Public Health Sciences Wake Forest School of Medicine Winston-Salem, NC 27157, USA No COI
REVIEW RETURNED	30-Dec-2012

THE STUDY	-The participants are not well described -The limitations of the study are not addressed -The reference list is incomplete
RESULTS & CONCLUSIONS	The results cannot be generalized. The literatured reviewed is incomplete.
GENERAL COMMENTS	In their manuscript, SK Virdee and co-authors addressed the question in the title “Would primary health care professionals prescribe a polypill to manage cardiovascular risk?” In semi-structured interviews of 16 of the 56 health care professionals from nine primary care practices in Birmingham, UK, three outcome measures were investigated – attitudes towards the use of a polypill, views on drug monitoring and factors influencing a willingness to prescribe a polypill. Although the study design and conduct were appropriate, the report raised two major concerns – relevance and generalizability. The broader context of the development of the polypill is not addressed. The major public health issue in low- and middle-income countries was until recently infectious diseases. Today the leading cause of death is non-communicable diseases including cardiovascular diseases (CVD). Under the leadership of the World Health Organization, efforts are now underway to reduce the burden of CVD in these countries. A central component of this program is the polypill. To limit the cost, the polypill relies on generic medications and the screening and the monitoring are limited. Ongoing major randomized clinical trials in these countries will determine the efficacy and safety of the polypill. Thus, the polypill was not primarily developed for use in the high-income countries. In other words, the relevance of an interview study limited to Birmingham, UK, can be questioned. A similarly designed study of health professionals in multiple low- and middle-income countries would have been both interesting and important. The small size of study, its limitation to a major city in the UK and the high refusal rate raise questions about how far the study findings can be generalized. They may or may not apply to other high-income countries with different health care systems. The concept of fixed combination polypills is likely difficult to sell in developed countries with compartmentalized delivery of health care.

REVIEWER	Alexander M Clark, Professor & Associate Dean, University of Alberta, Canada

REVIEW RETURNED	21-Jan-2013

THE STUDY	The paper's framing is not right for the qualitative methodology
RESULTS & CONCLUSIONS	This paper reports a small qualitative study that is focused on an important topic (views of the Polypill and its prescribing) but generates limited new information or insights. The framing of the paper is appropriate but also there are body of theory and research around knowledge to practice gaps / knowledge translation that are not well covered. More background could have been included on the prescribing rights and priviledges of the professional groups included. The method is a fairly generic qualitative descriptive study of health professionals' perspectives. The rationale for the selection of sites is provided and is apt. The methods are well detailed in terms of schedule development and consent. The use of member checking of the transcripts (page 10) is now quite dated due to a the large body of critique of this method of determining the validity of the interpretations and data produced in analysis. While not a fatal flaw, the rationale of this should be provided. What would the researchers have done if participants had not supported the analysis? While in the discussion the researchers claim the point of qualitative research is not to be generalizable, this is far less evident in their discussion and the implications section – which do seem to move beyond the sample.
REPORTING & ETHICS	Sample size is very small and the insights gleaned in the analysis fairly superficial and typical of past research. The themes are organized well – though the tendency to include numbers throughout it curious. With such a small sample size, these add nothing to the depth of the analysis or the theoretical transferability of the findings. This gives the appearance that the researchers do not understand qualitative methods well.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1
1. Additional references that would add weight to the paper are:
- CTT collaboration. Effects of lowering LDL in people at low risk of disease. Lancet 2012.
- Law et al. Use of BP lowering drugs in the prevention of cardiovascular disease. BMJ 2009.
- Yusuf et el. PURE study. Lancet 2011
- Elley et al. Efficacy and tolerability of 'polypills': a meta-analysis of RCTs. PLOS one 2012.
Thank you. We have added text to the first paragraph of the introduction citing these papers (references 9, 12, 13, 14).
New text reads:
However repeated surveys have shown many patients are not being treated as intensively as guidelines recommend.7-9 Furthermore, the majority of cardiovascular events occur in people not at high risk using conventional risk calculators.10 Therefore, offering a 'polypill' to everyone over a particular age (for example 55) has been proposed.11 The original idea involved a six component pill (three blood pressure lowering agents; cholesterol lowering agent; folate; and aspirin), but due to question marks over the efficacy of folate and the appropriateness of aspirin use for primary prevention, this now typically involves a single daily combined pill containing just blood pressure and

cholesterol lowering agents. Since the idea was first raised, the evidence base for the potential role of a polypill has grown. There is more evidence that the effect of blood pressure lowering on cardiovascular risk is independent of baseline blood pressure,12 and that reduction of LDL cholesterol is beneficial in those at low risk of vascular disease.13 Meta-analysis of early trials show that polypills do indeed lower blood pressure and serum cholesterol levels.14

9: Yusuf S, Islam S, Chow CK, et al. Use of secondary prevention drugs for cardiovascular disease in the community in high-income, middle-income, and low-income countries (the PURE Study): a prospective epidemiological survey. Lancet. 2011;378(9798):1231-1243.

12: Law MR, Morris JK, Wald NJ. Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies. BMJ (Clinical research ed). 2009;338:b1665.
13: Cholesterol Treatment Trialists C, Mihaylova B, Emberson J, et al. The effects of lowering LDL cholesterol with statin therapy in people at low risk of vascular disease: meta-analysis of individual data from 27 randomised trials. Lancet. 2012;380(9841):581-590.
14: Elley CR, Gupta AK, Webster R, et al. The efficacy and tolerability of 'polypills': meta-analysis of randomised controlled trials. PLoS One. 2012;7(12):e52145.

2. Authors should mention whether ethical consent was obtained to undertake the research and whether participants provided written informed consent to the research (and if not, why not).
Ethical approval to conduct the interviews was granted and consent from participants was obtained before interviewing. This was stated in the interview section of the method (lines 6-9).

3. Table 1 should be collated, rather than individual participant data.
We have adjusted the table of individual participant data as suggested (table 1).

4. It should be noted in the paper that in addition to blood pressure and lipid lowering medication, Wald and Law proposed the addition of aspirin and folate in their polypill.
We have added a sentence to the introduction (lines 9-13) noting this.
New text reads:
The original idea involved a six component pill (three blood pressure lowering agents; cholesterol lowering agent; folate; and aspirin), but due to question marks over the efficacy of folate and the appropriateness of aspirin use for primary prevention, this now typically involves a single daily combined pill containing just blood pressure and cholesterol lowering agents.

Reviewer 2
5. The participants are not well described.
We have adjusted the table of participant data (table 1) to make it clearer as per reviewer 1 (point 3). We feel that this, along with participants section of the results (lines 1-6), concisely describes the interviewees. However, we could add further detail should the editor require.

6. The limitations of the study are not addressed. The small size of the study, its limitations to a major city and the high refusal rate raise questions about how far the study findings can be generalized.
In the strengths and imitations section of the discussion, we have added to the limitations i.e. the study being carried out in a single major city and the high refusal rate (lines 5-8). As stated in this section, we cannot comment on the prevalence of the views of primary health care professionals or those from other healthcare systems.
New text reads:
Study participants were recruited from a single major city. Sixteen of the 50 approached were interviewed and we are not able to comment on how prevalent the views expressed in this study are in the wider population of primary health care professionals or those from other healthcare systems.

In terms of the sample size, this was a qualitative study for which the numbers were sufficient to achieve saturation as already stated (lines 11-12). We have not changed the text.

7. The reference list is incomplete.
The reference list has been checked and all references have been listed. We have also added additional references in response to points 1 and 9. (See references 9, 12, 13 and 14 in point 1).

8. The results cannot be generalised.
We agree and had stated in the strengths and limitations section of the discussion that the aim of qualitative research is not to be generalisable (lines 10-11). We also stated that we were unable to comment on how prevalent the views were of the wider population of primary health care professionals or those from other healthcare providers (lines 5-8). However, the study did allow an in depth exploration of primary health care professionals attitudes and interviews continued until no new themes emerged i.e. until theoretical saturation had been achieved. We have not changed the text.

9. The literature reviewed is incomplete.
Additional literature has been added as suggested by reviewer 1, point 1. (See references 9, 12, 13 and 14 in point 1).

10. The broader context of the development of the polypill is not addressed.
We agree that the development of the polypill within a broad context is not addressed. However, our study focussed on one context: the views of primary health care professionals and we have added text to clarify this at the end of the introduction (lines 35-39). We also agree further studies of health care professionals in other contexts would be interesting.
New text reads:
The polypill has been used in a range of settings. This paper reports on a study in Birmingham, UK, which used a qualitative description approach20,21 to investigate UK health care professionals' i.e. primary care physicians' and practice nurses' attitude towards using the polypill for cardiovascular disease prevention and the drug's practicality for monitoring and prescribing.

Reviewer 3
11. There is a body of theory and research around knowledge to practice gaps/knowledge translation that are not well covered.
This study was carried out at a time (as now) when the polypill is not available. We have referred to specific aspects of implementation research (viz the evidence that fixed dose combinations lead to higher adherence), but otherwise not drawn on this literature, as it is not central to the research question we are addressing. We have not changed the text.

12. More background could have been included in the prescribing rights and privileges of the professional groups included.
We have added a column to table 1 describing the number interviewees qualified to prescribe.

13. The use of member checking of the transcripts (page 10) is now quite dated due to the large body of critique of this method of determining the validity of the interpretations and data produced in analysis. While not a fatal flaw, the rationale of this should be provided. What would researchers have done if participants had not supported the analysis?
We are aware of the disadvantages of the method of member checking. However, we felt it important to use this technique as this was the first qualitative study on the polypill and the concept was new for interviewees. We have added text to support this in the analysis section of the method (lines 4-6). If participants had not supported our analysis, we would have revisited the data.
New text reads:
Although the advantages and disadvantages of this process have been documented,34 since this is

the first qualitative study on the polypill and it was a new concept for interviewees, it was felt important to do this.

14. While in the discussion the researchers claim the point of qualitative research is not to be generalisable, this is far less evident in their discussion and the implications section which do seem to move beyond the sample.
We agree with this and have qualified the text in the implications section of the discussion so that it is more specific to the respondents in our study (lines 1-3 and 6-8).
New text reads:
This study suggests despite potential acceptance of use of a polypill for secondary prevention, health care professionals interviewed remained concerned that monitoring should continue.
If a polypill is to be used in this way, based on our respondents views it is likely health care professionals would need to be convinced about the potential benefits of a drug based population approach to prevention.

15. Sample size is very small.
As mentioned in the strengths and limitations section of the discussion (lines 11-12), the sample size was sufficient to achieve saturation and is consistent with what is recommended in qualitative research (see reference 42 which supports this). We have not changed the text.
Reference 42:
Guest G, Bunce A, Johnson L. How many interviews are enough? An experiment with data saturation and variability. Field methods. Feb 2006;18(1):59-82

16. The insights gleaned in the analysis are fairly superficial and typical of past research.
We disagree. Our study is the first qualitative study on this topic area. Some of the findings do support those of quantitative research in other healthcare systems as discussed in the comparison with existing literature section of the discussion (lines 1-3 and 8-9). Our study adds data from another healthcare context to existing research.

17. The tendency to include numbers throughout is curious.
The numbers of respondents discussing each subtheme was reported in order to contextualise the findings and facilitate a comparison between respondents. This has been clarified in the key areas section of the results (lines 3-5).
New text reads:
The number of respondents discussing each subtheme is reported (denominator 16 participants) 37 in order to contextualise the findings and facilitate a comparison between respondents.