PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf**) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	A psycho-educational intervention for people at high risk of developing another melanoma: A pilot randomised controlled trial
AUTHORS	Dieng, Mbathio; Kasparian, N; Mireskandari, Shab; Butow, Phyllis; Costa, Daniel; Morton, Rachael; Mann, Graham; Menzies, Scott; Cust, Anne

VERSION 1 - REVIEW

REVIEWER	Jennifer L. Hay Memorial Sloan Kettering Cancer Center USA
REVIEW RETURNED	10-Mar-2017

GENERAL COMMENTS	This study reports on the findings of a small pilot study (12 participants exposed to the intervention, and 12 controls) examining the acceptability, feasibility, and short term (1 and 6 months) outcomes (e.g., fear of cancer recurrence, distress, quality of life outcomes) associated with the intervention. The intervention includes a psycho-educational booklet, a Cancer Council booklet on melanoma, and 3-5 telephone counseling sessions with a psychologist, based on short-term psychodynamic psychotherapy. Those in the control arm received the Cancer Council booklet on melanoma only. Findings indicate that participants who received the intervention were satisfied with it and perceived it to be helpful. While the study does look at psychological outcomes of the intervention, the sample size is too small for these analysis and I recommend elimination of this aspect from the paper. Additional specific comments are provided below. Background It is unclear why the study is including non-distressed participants. As nicely noted in paragraph 1, prior studies outline the important element of screening for distress first, so that only distressed individuals are offered treatment for distress. In the current study, no such screening was provided. While it might be possible to make the case that discussions with psychologists might be helpful for all cancer patients, it is important that distress interventions focus (for feasibility and scalability reasons, if nothing else) on those who report symptoms. The baseline level of symptoms was exceedingly low in this sample. Just as we would not treat pain in patients who do not endorse pain, this intensive intervention would be better deployed among those patients who need it. Further, the study recruited only those at early stages of disease (0-II), and only those with no history of prior psychiatric disorders. In addition to those reporting distress, it would seem useful to target those with more advanced disease, and at more risk of distress based on there prior

	psychiatric history. These would be the patients that would require intensive intervention as it would be more expectable that their distress would not remit spontaneously. The sampling here is counterintuitive. Methods How was feasibility operationalized and assessed? While I see that it is described broadly as difficulties, barriers, and resources, more clarity here would be useful, so that we could be clear about what the cut-offs are for feasible vs not feasible. For example, what level of retention would have indicated lack of feasibility? What is the rationale for the sample size? Results Page 16: Preliminary outcomes are all over the place, with either similar changes in intervention and control conditions, or changes in different directions that also differ at each time point. I think this is because many symptoms remit over time spontaneously (intervention or not), the small sample sizes, and the fact that these patients were not distressed at baseline. Little can be made of it with only 12 individuals in the intervention group, and so the statement in the Abstract, “preliminary outcome data suggests beneficial changes in fear of recurrence etc” is not strongly supported in this data and I therefore recommend this element of the paper be saved for future papers with larger samples collected. On page 19 (first para), the positive efficacy findings should also be tempered or eliminated. It does appear from the quotations that some of the beneficial effect of the intervention came from patients’ appreciation that they had time to ask questions of the psychologist. Is this finding relevant to their general cancer care, and a need for physicians to find time to address patient questions? How generalizable is an intervention that requires psychologists for delivery? If it is to be geared for individuals who are not distressed, could it perhaps be delivered by health educators?

REVIEWER	Sangchoon Jeon Yale School of Nursing, United States
REVIEW RETURNED	16-Apr-2017

GENERAL COMMENTS	#1. On page 16, authors should be more careful in description of the increases and decreases of outcomes with large standard deviations. For instance, they described increases of anxiety and stress in the intervention at 1 months although they had a very small mean changes with a large standard deviation. I believe those outcomes should be considered as no changes. I also recommend examining the changed outcomes over time using Mixed effect model, which will have more power by including repeated observations compared to the cross-sectional comparisons. Especially, it’s useful for this small sample size of pilot study. #2. Specify formula for 95% CI of Between-Group mean difference. #3. Effect size was calculated by dividing cross-sectional mean differences by standard deviations. Generally, it’s acceptable but I am concerning the baseline difference at baseline. For instance, the effect size of -0.33 in FCR severity at 6 months representing worsen FCR in the intervention arm even though it was decreased in the intervention (Mean change of -1.64 (SD=4.4) and not changed in the control (Mean change of 0.08 (SD=6.92). This opposite effect size is due to unbalanced FCR at baseline. (17.92 in the intervention vs.

	14.00 in the control). Due to the same reasons, other effect sizes also may not be representing the comparisons of changed outcomes. I would recommend calculating effect size by dividing delta (changed score from baseline) with a pooled standard deviation. Using the delta, the effect size on FCR is 0.29 (=1.72/Pooled SD) shows more decrease of FCR in the intervention. This calculation shows a great effect size on depression as well.

VERSION 1 – AUTHOR RESPONSE

Points raised by Reviewer 1

5. This study reports on the findings of a small pilot study (12 participants exposed to the intervention, and 12 controls) examining the acceptability, feasibility, and short term (1 and 6 months) outcomes (e.g., fear of cancer recurrence, distress, quality of life outcomes) associated with the intervention. The intervention includes a psycho-educational booklet, a Cancer Council booklet on melanoma, and 3-5 telephone counseling sessions with a psychologist, based on short-term psychodynamic psychotherapy. Those in the control arm received the Cancer Council booklet on melanoma only. Findings indicate that participants who received the intervention were satisfied with it and perceived it to be helpful. While the study does look at psychological outcomes of the intervention, the sample size is too small for these analysis and I recommend elimination of this aspect from the paper.
Thank you for this feedback, we have now removed the outcomes analysis from the manuscript.

Background
6. It is unclear why the study is including non-distressed participants. As nicely noted in paragraph 1, prior studies outline the important element of screening for distress first, so that only distressed individuals are offered treatment for distress. In the current study, no such screening was provided. While it might be possible to make the case that discussions with psychologists might be helpful for all cancer patients, it is important that distress interventions focus (for feasibility and scalability reasons, if nothing else) on those who report symptoms. The baseline level of symptoms was exceedingly low in this sample. Just as we would not treat pain in patients who do not endorse pain, this intensive intervention would be better deployed among those patients who need it. This issue was discussed substantially at the time of study design. Ultimately, a decision was made not to screen individuals for distress prior to study enrolment based on previous evidence accumulated by our team as well as others over the past 10 years showing that people at high risk of melanoma report a range of difficulties across various domains in addition to distress, including but not limited to: unmet health information needs; emotional and practical issues relating to melanoma diagnosis, treatment and ongoing clinical management; difficulties in communication with their healthcare team; anxiety; and challenges in accessing timely and appropriate psychological care. These difficulties are considered important to address in the context of a psycho-educational intervention, irrespective of self-reported distress scores and thus, a decision was made against screening in this trial. Moreover, fear of cancer recurrence was our primary outcome and there is very limited available evidence regarding the most appropriate and clinically-sensitive cut-off score as measured by the Fear of Cancer Recurrence Inventory.

7. Further, the study recruited only those at early stages of disease (0-II), and only those with no history of prior psychiatric disorders. In addition to those reporting distress, it would seem useful to target those with more advanced disease, and at more risk of distress based on there prior psychiatric history. These would be the patients that would require intensive intervention as it would be more

expectable that their distress would not remit spontaneously. The sampling here is counterintuitive.
We excluded people with active stage III melanoma or metastatic melanoma (stage IV) because research suggests that they have different psychosocial needs to stage 0/I/II patients, where the melanoma has been confined to a primary tumour only. To acknowledge this point we have added this sentence as the study limitation (page 4 and 17): “The exclusive recruitment of people who have had early stage melanoma limits generalisability and further research is needed to know if people with advanced melanoma have a similar response to the intervention.”
We are currently seeking funds to run a research project looking at the effect of a modified psycho-educational intervention for people with advanced melanoma.

Methods
8. How was feasibility operationalized and assessed? While I see that it is described broadly as difficulties, barriers, and resources, more clarity here would be useful, so that we could be clear about what the cut-offs are for feasible vs not feasible. For example, what level of retention would have indicated lack of feasibility?
A priori feasibility objectives were based on our previous experience: >30% consent, <15% lost to follow-up per group, 80% engagement rate (i.e., participation in all scheduled telephone sessions). Acceptability objectives were: average satisfaction scores ≥7/10, <15% negative qualitative responses within the questionnaire. We have added these details to page 12.

9. What is the rationale for the sample size?
See response to point 4 above.

Results
10. Page 16: Preliminary outcomes are all over the place, with either similar changes in intervention and control conditions, or changes in different directions that also differ at each time point. I think this is because many symptoms remit over time spontaneously (intervention or not), the small sample sizes, and the fact that these patients were not distressed at baseline. Little can be made of it with only 12 individuals in the intervention group, and so the statement in the Abstract, “preliminary outcome data suggests beneficial changes in fear of recurrence etc” is not strongly supported in this data and I therefore recommend this element of the paper be saved for future papers with larger samples collected. On page 19 (first para), the positive efficacy findings should also be tempered or eliminated.
As suggested, we have now removed the outcomes analysis from the manuscript.

11. It does appear from the quotations that some of the beneficial effect of the intervention came from patients’ appreciation that they had time to ask questions of the psychologist. Is this finding relevant to their general cancer care, and a need for physicians to find time to address patient questions?
We agree that this aspect is interesting, and to address this appropriately it will be included in a separate process evaluation of the larger study results.

12. How generalizable is an intervention that requires psychologists for delivery? If it is to be geared for individuals who are not distressed, could it perhaps be delivered by health educators?
It would be interesting to assess the effect of the intervention if it was delivered by trained nurses or other health professionals.

Indeed, although recommended in Australian clinical practice guidelines, psychological support (provided by a psychologist) is not currently part of routine care for people diagnosed with melanoma, and if research demonstrated a sustained effect when delivered by trained nurses or health educators that could perhaps facilitate implementation.

Points raised by Reviewer 2
13. On page 16, authors should be more careful in description of the increases and decreases of outcomes with large standard deviations. For instance, they described increases of anxiety and stress in the intervention at 1 months although they had a very small mean changes with a large standard deviation. I believe those outcomes should be considered as no changes. I also recommend examining the changed outcomes over time using Mixed effect model, which will have more power by including repeated observations compared to the cross-sectional comparisons. Especially, it's useful for this small sample size of pilot study.
Based on reviewer 1's advice, we have now removed the outcomes analysis from the manuscript.

14. Specify formula for 95% CI of Between-Group mean difference. Based on reviewer 2 advice we have now removed the outcomes analysis from the manuscript.

15. Effect size was calculated by dividing cross-sectional mean differences by standard deviations. Generally, it's acceptable but I am concerning the baseline difference at baseline. For instance, the effect size of -0.33 in FCR severity at 6 months representing worsen FCR in the intervention arm even though it was decreased in the intervention (Mean change of -1.64 (SD=4.4) and not changed in the control (Mean change of 0.08 (SD=6.92). This opposite effect size is due to unbalanced FCR at baseline. (17.92 in the intervention vs. 14.00 in the control). Due to the same reasons, other effect sizes also may not be representing the comparisons of changed outcomes. I would recommend calculating effect size by dividing delta (changed score from baseline) with a pooled standard deviation. Using the delta, the effect size on FCR is 0.29 (=1.72/Pooled SD) shows more decrease of FCR in the intervention. This calculation shows a great effect size on depression as well.
Thank you for the suggestion; however based on reviewer 1's advice, we have now removed the outcomes analysis from the manuscript.

Reference:
1. Moore CG, Carter RE, Nietert PJ, et al: Recommendations for planning pilot studies in clinical and translational research. Clin Transl Sci 4:332-7, 2011

VERSION 2 – REVIEW

REVIEWER	Sangchoon Jeon Yale University, United States
REVIEW RETURNED	11-Jul-2017

GENERAL COMMENTS	No more questions on statistical issues.