Author’s response to reviews

Title: Short and Long-term Barriers and Facilitators of Skin Self-Examination Among Individuals Diagnosed with Melanoma

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Response to Reviewers’ Comments:
BCAN-D-19-02930: Short and Long-term Barriers and Facilitators of Skin Self-Examination Among Individuals Diagnosed with Melanoma
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BMC Cancer

REVIEWER #1: DR. JUNE K. ROBINSON

GENERAL COMMENTS

Reviewer #1, General Comment #1: The manuscript provides an excellent review of the SSE literature, but the literature review is not current in all aspects.
Our response to Reviewer #1, General Comment #1: We updated our background section, including clarifying information and claims about the current state of the literature, as per suggestions from Reviewer 2 (e.g., Reviewer 2, Comments # 2-18).
Reviewer #1, General Comment #2: This is an observational study of customary clinical practice using standardized dermatologic education on skin cancer prevention with a surveys of melanoma survivors, who provided self-reported outcomes. The content of this education needs to be stated in the methods. Skin Cancer Prevention programs as currently stated in the methods may be limited to sun protection with a cursory mention of SSE. Such programs do not use a structured SSE training program as an intervention. The reader is informed about the content of the education in the discussion on page 15 lines 53-57.

Our response to Reviewer #1, General Comment #2:
In the “method” section, “participants and procedures” subsection we added the following paragraph about the educational session:
- “The dermatological educational session was delivered by three research assistants with backgrounds in medical sciences, nursing, and psychology, all of whom were trained by a dermatologist on the research team (BW). The educator briefly introduced herself, stated the purpose of the session (“how to best examine one’s skin for the early signs of melanoma”), explained the ABCDE criteria for the identification of problematic moles, illustrated how to systematically check the skin (checking all body parts with the help of another person), and provided take-home materials (e.g., body map diary, ABCDE book mark). A detailed document about the content of the educational session is available online at https://osf.io/ftw6v/?view_only=3eaa58a6f4654bd3af2064bbeceb15ad”.

Reviewer #1, General Comment #3: The finding that SSE is maintained over 24 months with the greatest performance in the immediate usual care education supports the work of others but does not "break new ground".

Our response to Reviewer #1, General Comment #3:
The reviewer is correct in this overall assessment of the manuscript. We hope that our reporting of our results and the contextualization of our findings within the current melanoma prevention field is accurate and our claims do not overextend the impact of our findings.

Reviewer #1, General Comment #4: The authors refer to a number of their own unpublished works about development of measures, and briefly state the five items inquiring about separate body areas, which are grouped in a manner that is not supported by SSE performance of trained melanoma survivors and their skin check partners (Robinson JAMA Dermatol 2016, Turrisi JAMA Dermatol 2015). As an example, if in page 10 line 50, the subject was asked about examination of head and neck which included face, neck and scalp, then the subject would have difficulty responding as SSE of the face (easy to see alone) is more frequent than that of the scalp (difficult to see alone).

Our response to Reviewer #1, General Comment #4: The reviewer is correct in identifying a limitation of our assessment of SSE, particularly about the item #1 which inquires about the examination of the “face, neck, and scalp” in one item – while the face can be easily inspected individually, the inspection of the scalp and neck areas would likely require the help of another person or the use of two mirrors. Unfortunately, we had planned and administered this item in this fashion to all participants and could not separate post-hoc the answers to checking of the face from those referring to the neck and scalp. This is a limitation of our assessment measure for SSE, which we mentioned in the discussion section. However, we adjusted the answers to this item (#1) to match the highest score reported on either the item inquiring about “getting help from another person during the skin exam” (item #6) OR the item inquiring about “using two mirrors during the skin exam” (item #7) in order to correct for over-reporting of checking the face area versus the neck/scalp areas, which require external help.

- We realized that the submitted manuscript stated that we corrected the scores on items (3, 4, 5)
against the highest scores obtained on items 6 or 7, when in fact it should have been stated that scores for items 1 (face/neck/scalp), 4 (upper back), and 5 (lower back) were corrected. We corrected this error.

- We also decided to include a subsection entitled “Scoring of the SSE Behaviour Scale” to facilitate a more transparent reporting of the information about how the items were initially administered versus how they were scored/analyzed and the rationale for it.

Reviewer #1, Concern #1: The following two areas of concern decrease the importance and reliability of the data presented. Retention at 3-6 months was 40% and at 24 months was 21%, thus, the responses are likely to be skewed in the direction of responses from those who are performing SSE as those not performing SSE dropped out.

Our response to Reviewer #1, Concern #1: The reviewer is raising a great point, which we believe we stressed adequately in the limitation subsection of the discussion. We added a CONSORT flowchart, which more transparently reports the retaining dates throughout the different phases of the study (see also our response to Reviewer #1, Comment #2).

Reviewer #1, Concern #2: Documentation of delivery of education and reminders in the "naturalistic setting" should be possible, e.g. number of times the patient received a total body skin exam with a dermatologist during the 24 month period of the study, and physician reminders to perform SSE as perceived by patients during the total body skin exam. Confounding of the results by the dermatologic care received is alluded to in the discussion (page 16 lines 40-46).

Our response to Reviewer #1, Concern #2: We agree with the reviewer that data on the number of dermatological exams, including demonstration and reminders/prompts for SSE, received during the study period have been extremely useful. This is indeed a limitation of the study. To clarify this important point, we included the following statement in the limitation section:

- “Further, given that we did not collect data systematically on the number of dermatological appointments that occurred throughout the duration of our study, it is impossible to accurately assess the impact of clinical skin exams on the practice of skin self-exams. Furthermore, it is also practically impossible to speculate on the degree to which the clinical exam might have acted as a reminder or booster for participants’ own practice of SSE.”

SPECIFIC COMMENTS:

Reviewer #1, Comment #1: This observational study with longitudinal assessment of melanoma patients does not consider non-melanoma skin cancer patients or their customary education in SSE, thus, reference to all types of skin cancer on page 6 lines 3-5 (the first sentence) should be deleted.

Our response to Reviewer #1, Comment #1: We deleted the first sentence, which referred to all skin cancers, and replaced it with the following sentence about melanoma:

- “Melanoma is the 5th most common cancer in the United States (Howlader et al., 2016) and the 7th in Canada (Canadian Cancer Statistics Advisory Committee, 2019).”

Reviewer #1, Comment #2: A participant flow chart is provided in the Appendix rather than as a CONSORT Diagram in the body of the printed publication. This is peculiar.
Our response to Reviewer #1, Comment #2: We replaced the existing participation table with a STROBE Flowchart Diagram, as appropriate for reporting participation in observation studies.

Reviewer #1, Comment #3: The first sentence of the discussion is troubling. The RCT by Robinson et al (JAMA Dermatol 2016 not cited in the references) reports follow-up through 24 months. While the authors seek to differentiate their work as follow-up in "best-practice" care from the RCT, they should at least acknowledge the published RCT.
Our response to Reviewer #1, Comment #3: We added the following sentence at the beginning of the discussion section, immediately after the opening statement:

- “The only other study to report a 24-month follow-up among melanoma patients is a randomized controlled trial testing the efficacy of delivering a melanoma prevention message via three different modalities against usual care (Robinson, 2016)”.

Reviewer #1, Comment #4: Discussion: limitations - move the confounding of the results by the dermatologic care received (page 16 lines 40-46) to the limitations section.
Our response to Reviewer #1, Comment #4: We added the following statement to the limitations section (also mentioned under Reviewer #1, Concern #2):

- “Further, given that we did not collect data systematically on the number of dermatological appointments that occurred throughout the duration of our study, it is impossible to accurately assess the impact of clinical skin exams on the practice of skin self-exams. Furthermore, it is also practically impossible to speculate on the degree to which the clinical exam might have acted as a reminder or booster for participants’ own practice of SSE.”

Reviewer #1, Comment #5: Recommendation re future intervention studies (Discussion page 18, lines 7-12) should note that the recommended study was done as an RCT.
Our response to Reviewer #1, Comment #5: We added the following sentence to reflect the fact that some trials exist which have tested some of the recommendations we provided:
- “While some of these recommendations have already been used and tested (e.g., Robinson et al, 2016), future research is needed to optimize these recommendations and instructions for different at-risk populations”.

REVIEWER #2: DR. CAROLINE WATTS, PHD

This paper describes the short-term and long-term predictors of skin self-examination. I like the way you defined two groups based on the thoroughness of examination and your analysis appears well done. I think this is a paper of interest to health care professionals with an interest in melanoma research. There are quite a few points, which require clarification in the Background section of the manuscript, which I have outlined below. I have some additional questions regarding the manuscript.

Reviewer #2, Comment #1: Did the authors consider asking about partner status and do they think this may have an effect on SSE?
Our response to Reviewer #2, Comment #1: The reviewer is raising a very important issue. It is possible that not having a life partner (or someone else who could provide help) could make it more difficult for someone to skin-check hard to reach areas. We anticipated this problem during the design phase of the study and included in the dermatological education session instructions/recommendations...
that participants conduct SSE with the help of another person (life partner, child, friend, or someone else) and we also created specific items as part of the SSE assessment that inquired about “getting help from someone else” or “using two mirrors” to check the skin on hard to reach body areas (please also see our response to Reviewer #1, General Comment #4 regarding the scoring of the SSE measure; please also see our response to Reviewer #1, General Comment #2 regarding the content of the educational session).

Reviewer #2, Comment #2: Did the authors check the dates for follow-up appointments and could this have influence adherence to SSE? And did patients with thicker melanomas have more frequent clinician follow-up?
Our response to Reviewer #2, Comment #2: This is another great point raised by this reviewer. Unfortunately we did not collect data on the medical appointments that occurred throughout the duration of our study. We mentioned this as one the limitations for this study (please see our response to Reviewer #1, concerns #2).

Reviewer #2, Comment #3: Could the authors provide some thoughts related to their experience why the comprehensiveness of SSE was maintained but yet there was decreasing frequency of SSE over time.
Our response to Reviewer #2, Comment #3: Based on the current analyses, which we planned a priori, it seems that comprehensive SSE in the short and long run is primarily related to past higher intentions and self-efficacy for SSE whereas, optimal, monthly SSE in the short and long term is related to past self-efficacy alone. Unfortunately, the higher than anticipated attrition rate and the current design (cannot establish cause and effect) did not allow us to investigate in more depth the changes in SSE as a function of changes in our predictor variable set.

Reviewer #2, Comment #4: Could the authors expand on the measures motivational interviewing and implementation intentions to address decreasing frequency of SSE over time.
Our response to Reviewer #2, Comment #4: We have added more detail in the Clinical Implications and Directions for Future Research subsection of the discussion about how Motivational Interviewing and Implementation Intentions interventions could potentially foster SSE behaviour in the short and long term:

- “To facilitate the setting of intentions to perform skin self-exams and subsequently ask for clinical exams, future studies could employ Motivational Interviewing strategies (Rollnick, Miller, & Butler, 2008) to investigate personal desires and motivations (pro’s and con’s) to perform SSE, individual resources to support a long-term SSE practice (e.g., spousal support, knowledge of prevention and self-efficacy for SSE) and to address individual barriers, current and anticipated, to the adoption of skin cancer screening behaviors. In addition, interventions focused on effective goal setting, such as implementation intentions (Gollwitzer, 1993) could facilitate a long-term maintenance of SSE practice by creating individualized plans for when, how, where to perform the SSE at different points in the future”.

COMMENTS REGARDING THE BACKGROUND

Reviewer #2, Comment #5: Page 5, paragraph 3, "in the last 3 months and were …" . The and needs to be removed.
Our response to Reviewer #2, Comment #5: We have removed the “and”.

Reviewer #2, Comment #6: Page 5, paragraph 4, Could the authors review if you need the "post" descriptor as all intervals are following the intervention and implicit.
Our response to Reviewer #2, Comment #6: We have made this change. The sentence now reads:

- “Optimal SSE was higher at 3 months (59%) compared to 12 (46%) and 24 months (34%), with key predictors including self-efficacy and intentions to perform SSE and male sex at 3 months post; self-efficacy and reliance on medical advice at 12 months; and (lower) education and self-efficacy at 24 months.”

Reviewer #2, Comment #7: Page 6, line 5 Could the authors clarify who is projecting the statistics or clarify if the estimate is for invasive or in situ melanoma, and also for the melanomas referred to on line 11.
Our response to Reviewer #2, Comment #7: Neither sources cites for line 5 and line 11 estimates specify if they are referring to invasive or in situ melanoma, and we assume that the prevalence estimates include both. We have clarified the statement in line 5, and updated the statistics to reflect 2019 prevalence estimates. The sentence how reads:

- “The National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) program projected that in 2019, there will be 96,480 new cases and 7,230 deaths from melanoma in the US (Howlader et al., 2016).”

We have also modified line 11 to clarify the source of the statistics:

- “The Canadian Cancer Society estimates that in Canada there were 6,800 new cases and 1,150 deaths from melanoma in 2015.”

Reviewer #2, Comment #8: Page 6, line 14. I was surprised to read that melanoma tumours grow faster than other tumors. Could the authors please reference or clarify this statement.
Our response to Reviewer #2, Comment #8: We corrected our statement about melanoma growing faster than other cancers, which was indeed incorrect, to reflect that melanoma metastasizes when much smaller than other cancers. The relevant sentence now reads:

- “Melanoma is one of the most deadly human cancers and can metastasize when the primary tumour is only 1 mm in diameter, compared to most human cancers which metastasize when they are 1cm (Barskey et al., 1997, Safarians, Sternlight, Freiman, Huaman, & Barsky, 1996)”

Reviewer #2, Comment #9: Page 6, line 25. Survival rates for in situ and Stage II melanomas are very different and AJCC Melanoma Staging estimates would be useful to refer to.
Also could the authors review the definition of distant disease as Stage III is usually defined as characterised by regional rather than distant spread, which defines Stage IV.
Our response to Reviewer #2, Comment #9: We have consulted a review of AJCC melanoma staging estimates to correct this statement, and the revised statement no longer references regional vs. distant disease, instead it now reads:

- “Melanoma is one of the most deadly human cancers and can metastasize when the primary tumour is only 1 mm in diameter, compared to most human cancers which metastasize when they are 1cm (Barskey et al., 1997, Safarians, Sternlight, Freiman, Huaman, & Barsky, 1996)”
“The 5-year survival rates vary depending on stage at diagnosis, and decline with more advanced staging at diagnosis: 95-100% stage I, 65-92.8% stage II, 41-71% stage III, and 9-28% stage IV (Costa Svedman et al., 2016).”

Reviewer #2, Comment #10: Page 6, line 29 and line 35. There are two sentences describing the increased risk of subsequent primary for melanoma survivors; a 9 fold increase or 60% increased risk. Could you adjust the text to clarify for the reader.
Our response to Reviewer #2, Comment #10: We have removed the sentence referring to 60% increased risk: “A study from Alberta, Canada, found that melanoma survivors have a 60% increased risk to develop a second primary melanoma compared to people without a prior melanoma (Jung, Dover, & Salopek, 2014)”

Reviewer #2, Comment #11: Page 6, line 41. Could the authors review the sentence where reducing mortality is based on early diagnosis of premetastatic tumors.- if premetastatic then by definition is early.
Our response to Reviewer #2, Comment #11: We have removed the word “premetastatic” to eliminate this redundancy. The first part of the sentence now reads:
- “There is consensus within the clinical and scientific communities that 1) intervention strategies designed to reduce melanoma-related mortality must focus on early diagnosis of cancerous tumours…”

Reviewer #2, Comment #12: Page 6, line 49. Could the authors review the sentence "Because melanoma develops within a pre-clinical phase, it is amenable to early detection" is confusing as some melanomas are difficult to detect and an earlier sentence said that melanomas grow faster than other tumors and metastasize when they are only 1mm in depth.
Our response to Reviewer #2, Comment #12: We appreciate this comment and have revised the sentence to reflect that not all melanomas can be detected before metastasis. The sentence now reads:
- “Because some melanomas develop with a visible, pre-clinical phase, they can be amenable to early detection via visual inspection of the skin, by physicians and lay persons (Friedman, Rigel, & Kopf, 1985).”

Reviewer #2, Comment #13: Page 7, line 48. Could the authors review the sentence "...it is well known that SSE's are related to better prognosis" doesn't make sense as a sentence. Also aren't clinician-detected melanomas thinner that patient detected melanomas and Breslow depth of lesion is related to prognosis.
Our response to Reviewer #2, Comment #13: We have revised the part of the sentence that was confusing. We did not expand the statement to clinician-detected melanomas because the focus of the paragraph is on SSE. The sentence now reads:
- “Even though cutaneous melanomas are generally readily visible on the skin surface and individuals who perform SSE have a better prognosis than those who do not…”
Reviewer #2, Comment #14: Page 7, line 48. Could the authors consider the addition of "generally" to the sentence "...readily visible on the skin surface" as some melanomas may not be easy to detect due to body site.
Our response to Reviewer #2, Comment #14: We have made the requested change (see sentence in previous comment).

Reviewer #2, Comment #15: Page 7, line 57. Could the authors clarify what they mean in the sentence "...vary by the modality of asking about the exam and the time frame of assessment."
Our response to Reviewer #2, Comment #15: We modified the sentence in question to more clearly reflect our intended message. The sentence now reads:
- "Reported SSE rates among melanoma survivors vary based on the definition of SSE used and the timeframe of assessment (Coroiu et al., accepted).”

Reviewer #2, Comment #16: Page 8, line 3-Page 8 Line 14. Could the authors please provide some interpretation around these results.
Our response to Reviewer #2, Comment #16: We have added some interpretation. The last two sentences of the paragraph now read (with added text in bold):
- “Coups and colleagues (Coups, Manne, Stapleton, Tatum, & Goydos, 2016) found that, although 72% of 176 melanoma patients had performed SSE during the last 2 months, only 14% had examined their whole body. These fluctuating rates of SSE reported in the literature illustrate a trend whereas only a small proportion of patients seem to be performing whole body SSE regularly, as per clinical recommendations; by missing certain body parts during the skin exam, opportunities for early detection of melanoma are also missed”.

Reviewer #2, Comment #17: Page 8, line 44. Can the authors elaborate on the effect of level of anxiety on SSE?
Our response to Reviewer #2, Comment #17: We clarified our claim further and the sentence now reads:
- “There is also preliminary evidence that cancer-related, occupational and financial distress were associated with increased frequency of SSE among melanoma survivors (Körner, Augustin, & Zschocke, 2011)”.

Reviewer #2, Comment #18: Page 7, line 48. Could the authors consider the addition of "morbidity and" to the sentence "...lower melanoma related mortality."
Our response to Reviewer #2, Comment #18: We have made this change: “In sum, there’s a strong argument from the empirical literature that the early detection of melanoma is associated with less advanced disease and as such with lower melanoma-related morbidity and mortality.”

ADDITIONAL COMMENTS ON THE MANUSCRIPT.
Reviewer #2, Comment #19: Page 14, line 31. Can you check the variables in the table match the...
Our response to Reviewer #2, Comment #19: We have added clarification to make sure the variables in the tables match the manuscript. We have added the names/acronyms of the measures used for specific constructs in-text on page 14. We have also made some modifications to the legend of Table 3 to match the changes in the results section of the manuscript.

Reviewer #2, Comment #20: Page 14, line 50 and 52. Can the authors check if the same variable "advanced stage" is mentioned twice.
Our response to Reviewer #2, Comment #20: We would like to confirm that the variable referring to “melanoma stage” was mentioned three times in the paragraph in question because it was a significant predictor for SSE comprehensiveness at 3, 12 and 24 months follow-up.

Reviewer #2, Comment #21: Page 17, line 50. Demo should be demonstration
Our response to Reviewer #2, Comment #21: We have made the requested change.

Reviewer #2, Comment #22: Could the authors check Table 1. I believe this table requires review as it contains demographic data with quartiles and results in different columns. Usually it is good to know if the females and male characteristics are similar or different. Stage at diagnosis is presented in one column. It is unclear why the quartiles are presented for the demographic data and what they mean for the other variables. If this could be clarified in the table this would be informative to the reader. I cannot see a title on my version but may be related to the printout.
Our response to Reviewer #2, Comment #22:
We have carefully reconsidered the structure of Table 1 in light of Reviewer 2’s comments. However, we decided not to make any modifications to the information presented in the table because we believed that some readers will find the quartile data to be informative relative to the distribution of the demographic and baseline data for our key study variables. We edited the title of the table to more accurately reflect the data presented, as follows:

- “Table 1. Characteristics of the Study Sample, including Demographic Characteristics and Baseline Data for the Study Measures (n=145)”.