Secondary Prevention of Melanoma via Skin Self-Examination among At-Risk Individuals:

An Investigation of Primary and Secondary Sources of Evidence

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Abstract

Melanoma is the most lethal type of skin cancer, but survival rates are excellent when the disease is detected early and the tumour is removed. Although melanomas grow faster than other skin cancers and can metastasize when only 1 mm in depth, they develop with a visible pre-clinical phase, which makes them amenable to early detection via inspection of the skin. Periodic examination of the skin is important, especially for individuals who have an increased risk to develop this disease, as it can lead to the early identification of cancerous lesions, timely treatment and improved survival. Self-examination of the skin conducted in tandem with the clinical skin exam by a health care professional appears to be a sensible and effective approach to the early detection of melanoma. However, many individuals at high risk do not perform skin self-examination despite medical recommendations. The goals of this doctoral thesis were to a) identify interventions that are effective at promoting melanoma early detection behaviours and b) identify barriers and facilitators of skin self-examination (SSE) among individuals at increased risk for developing melanoma.

Manuscripts 1 and 2 pertain to a systematic review of 12 randomized controlled trials (RCT) of behavioural interventions with individuals at increased risk for melanoma. Eligible behavioural interventions were those that included materials or teaching sessions on how individuals can check their skin for problematic lesions and how /when to ask for medical evaluation of lesions. Manuscript 1 aimed to summarize the various conceptualizations (definitions and operationalizations) of skin self-examination behaviour (or SSE)[1], as it was used in the identified RCTs. The study found that SSE behaviour was assessed primarily via single items and there were variations across trials in how the items were phrased, scored, and used in analyses. We also found that there is only minimal evidence supporting the validity and reliability of the items used to assess SSE behaviour. Manuscript 2 aimed to evaluate the effect of behavioural interventions on three outcomes, melanoma-related mortality, melanoma early detection, and preventive health behaviours, including skin self-examination (SSE), partner-assisted skin examination (PASE), and clinician-administered skin examination (CSE).

[1]SSE and SSE behavior will be used interchangeably throughout the thesis document.

Early detection of melanoma was conceptualized as thin (early stage, 0-II) versus thick (advanced stage; III-IV) lesions at diagnosis. This study found that currently there are no behavioural trials that evaluate melanoma-related mortality or early detection of melanoma. The 12 eligible trials evaluated the effect of interventions on preventive behaviours: SSE, PASE, and CSE. The study found some methodological heterogeneity between the trials and the risk of bias was unclear for most trials, due to incomplete reporting. Meta-analysis including studies with comparable intervention components (i.e., provision of tailored information on personal risk and recommendations on how to perform SSE) and similar methods of assessing SSE (i.e., percentage of individuals who performed SSE in the 4-6 months post the intervention) found a small significant effect on SSE; the effect on PASE and CSE was not significant.

Manuscript 3, which was an observational study with longitudinal follow-up, investigated the short- and long-term predictors of SSE in a sample of melanoma survivors, who are at increased risk for subsequent melanomas. All of the participants recruited in the study were administered a brief educational session on SSE, i.e., how to check their skin for problematic, potentially cancerous lesions. Predictors of SSE were assessed at 3, 12, and 24 months post the educational session. The study found that SSE behaviour decreased over time, from 3 month to 24 months after the educational session. Intentions to perform SSE predicted the comprehensiveness of the skin exam (i.e., checking the entire body, comprised of 5 body parts) at both short- and long-term follow-ups. Self-efficacy for SSE predicted optimal SSE (i.e., checking of the entire body on a monthly basis, as recommended during the educational session and as per current guidelines of care for melanoma survivors) at both short- and long-term follow-ups.

Results from these studies fill current gaps in the melanoma prevention literature by a) synthesizing the current modalities of operationalizing SSE behavior in melanoma prevention trials, and by making a call for future research to investigate the validity of SSE scales; b) synthesizing the effect of behavioural interventions on melanoma preventive behavior among at-risk individuals; and c) identifying the strongest short- and long-term predictors of SSE following a standardized educational session on SSE.

Résumé

Le mélanome est le type de cancer de la peau le plus mortel, mais les taux de survie sont excellents lorsque la maladie est détectée tôt et que la tumeur est retirée. Bien que les mélanomes se développent plus rapidement que d'autres cancers et peuvent se propager dès que la tumeur mesure seulement 1mm d'épaisseur, ils se développent avec une phase pré-clinique visible qui peut être identifié rapidement par le biais d'une inspection de la peau. Un examen de la peau périodique est important, surtout pour les individus qui présentent un risque accru de développer cette maladie, afin de permettre l'identification précoce des lésions cancéreuses, un traitement rapide, et un taux de survie plus élevé. L'auto-examen de la peau effectué en tandem avec l'examen clinique de la peau semble être une approche pratique et efficace pour la détection précoce d'un mélanome. Cependant, plusieurs personnes à haut risque n'effectuent pas d'auto-examens de la peau malgré ces recommandations médicales. Les objectifs de cette thèse doctorale étaient : a) d'identifier des interventions efficaces visant à faciliter les comportements de détection précoce du mélanome et b) d'identifier les obstacles et les facilitateurs d'auto-examens de la peau chez les personnes avec un risque plus élevé de développer un mélanome.

Les manuscrits 1 et 2 portent sur une revue systématique d'essais contrôlés randomisés (ECR) d'interventions comportementales auprès d'individus présentant un risque accru de mélanome. Les interventions comportementales éligibles devaient inclure des matériaux ou des séances d'enseignement pour montrer aux individus comment vérifier leur peau pour des lésions problématiques et comment/quand demander un avis médical pour les lésions. Le manuscrit 1 avait pour but de synthétiser les différentes conceptualisations (définitions opérationnelles) des comportements d'auto-examen de la peau utilisées dans les ECR identifiés. L'étude a révélé que les comportements d'auto-examen de la peau était évaluée principalement avec des items singuliers et qu'il y avait des différences dans la façon dont ces items étaient formulés, scorer et utilisés dans les analyses. Nous avons également trouvé peu de preuves pour appuyer la validité et de la fidélité des items utilisés pour évaluer les comportements d'auto-examen de la peau. Le manuscrit 2 visait a évalué l'effet des interventions comportementales sur trois résultats : la mortalité liée au mélanome, la

détection précoce du mélanome, et les comportements préventifs pour la santé, incluant l'auto-examen de la peau, l'examen de la peau assisté par un partenaire, et l'examen de la peau effectué par un médecin. La détection précoce du mélanome a été conceptualisée comme étant des lésions mince (stade précoce, 0-II) versus épais (stade avancé, II-IV) lors du diagnostic. Cette étude a révélé qu'il n'existe présentement aucun essai comportemental évaluant la mortalité liée au mélanome ou la détection précoce du mélanome. Les 12 ECR éligibles ont évalués l'effet des interventions sur les comportements de prévention : l'auto-examen de la peau, l'examen de la peau assisté par un partenaire, et l'examen de la peau effectué par un médecin. L'étude a identifié de l'hétérogénéité méthodologique entre les ECR et le risque de biais était vague dû au reportage incomplet. Une méta-analyse incluant des études avec des interventions comparables (c.-à-d. la provision d'information personnalisé sur le risque et de recommandations sur comment effectué l'auto-examen de la peau) et des méthodes similaires pour évaluer l'auto-examen de la peau (c.-à-d. le pourcentage d'individus qui ont effectué des auto-examens de la peau dans les 4 à 6 mois suivant l'intervention) a trouvé petit effet significatif sur l'auto-examen de la peau. L'effet sur l'examen de la peau assisté par un partenaire et l'examen de la peau effectué par un médecin n'était pas significatif.

Le manuscrit 3, une étude observationnelle avec suivi longitudinal, a examiné les facteurs prédictifs à court et à long terme de l'auto-examen dans un échantillon de patients atteints de mélanome ayant un risque plus élevé pour des mélanomes futurs. Tous les participants recrutés pour l'étude ont reçu une brève séance éducative sur l'auto-examen de la peau, c.-à-d. les méthodes pour identifier des lésions problématiques et potentiellement cancéreuses sur la peau. Les indicateurs d'auto-examen de la peau ont été évalués a 3, 12, et 24 mois suivant la séance éducative. L'étude a révélé que les comportements d'auto-examen diminuent avec le temps, de 3 à 24 mois après la session éducative. L'intention de procéder à l'auto-examen de la peau prédit l'exhaustivité de l'examen cutané (c.-à-d. la vérification des 5 parties du corps composant l'ensemble du corps) lors de suivis à court et à long terme. L'auto-efficacité pour l'auto-examen de la peau prédit une fréquence d'auto-examen optimal (c.-à-d. une vérification mensuelle de l'ensemble du corps, comme recommandé par la

séance éducative et par les guides pratiques pour le soin des survivant du mélanome) lors d'un suivi à court et à long terme.

Les résultats de ces études vont combler les lacunes dans la littérature de prévention du mélanome a) en synthétisant les façons d'opérationnaliser les comportements d'auto-examen de la peau dans les ECR de prévention du mélanome et en faisant appel pour les futures études d'explorer la validité des échelles d'auto-examen de la peau ; b) en synthétisant l'effet des interventions comportementales sur les comportements de prévention du mélanome parmi les individus a risque élevés pour des mélanomes ; et c) en identifiant les indicatifs à court et à long terme les plus puissants pour l'auto-examen de la peau après un séance éducative sur l'auto-examen de la peau standard.

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I would like to thank my co-authors for their contribution to the manuscripts included in this thesis. My special thanks to Chelsea – I could not have completed this thesis without your help! I would also like to acknowledge the funding agencies that made my research possible over the years, the Canadian Institutes of Health Research and the Fonds de Recherche du Québec-Santé.

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Finally, I would like to thank my parents, my sister, and my family in Romania, for their love and support over the years, for providing me with the best opportunities while growing up and well into adulthood, and for valuing educational pursuits over many others. In my research endeavors, I draw upon my personal experiences with my grandparents who managed their chronic illnesses without the medical advances and technologies we have today. They are my inspiration for pursuing health research and I wish I could share this accomplishment with them.

Contribution to Original Knowledge

This thesis builds on an existing body of knowledge regarding the secondary prevention of melanoma through early detection. The thesis made contribution to three distinct but related areas within the melanoma prevention literature. First, it provided a comprehensive and replicable review of the operationalization (including definition and measurement) of skin self-examination (or SSE), which is a melanoma preventive health behaviour. Using a pre-registered methodology, we reviewed several clinical trials that used SSE as a primary outcome and identified some variability in how SSE behaviour was conceptualized and measured. This work provides a rationale for the wide variability in SSE prevalence rates reported for similar populations in the melanoma prevention literature: the existing prevalence rates are directly impacted by the method used to assess SSE behaviour. Second, this thesis includes a review of the empirical evidence on the efficacy of behavioural interventions conducted with individuals at increased risk for melanoma on health (melanoma-related mortality) and health-related outcomes (melanoma early detection, melanoma preventive behaviours). In the last two years, two other reviews were published that investigated the effect of melanoma prevention interventions. Our review differs from these previous reviews in several respects:

a) our population inclusion criteria comprised of individuals at an increased risk for melanoma compared to the general population (e.g., individuals with a personal or familial risk, individuals with a specific phenotype/skin type), whereas previous reviews included any populations (Henrikson et al., 2018) or just individuals with a personal or familial history (Wu et al., 2016). Our rationale for excluding general population studies and only including populations from previously identified at-risk categories was that the prevention needs and the medical recommendations for risk assessment and screening are similar across at-risk groups but different from the recommendations for the general population (i.e., In North American, there are no recommendations for periodic screening for skin cancer)

b) our review only included randomized controlled trials (RCT), whereas the other two reviews included other study designs in addition to RCTs. The aim of our review was to identify the most efficacious behavioural

interventions that have an impact on three outcomes of interest (mortality, melanoma early detection, and melanoma prevention behaviours) and RCTs are considered using the best research design to address this aim.

c) our review methodology was pre-registered, and we conducted the review as per protocol. Consequently, we thoroughly assessed the risk of bias across the included trials and carefully evaluated the clinical and methodological heterogeneity across the eligible trials. In doing so, we were able to provide a more focused and in-depth picture of the existing behavioural interventions compared to what previous reviews reported.

Last, this thesis includes an empirical examination of short (3 months) and long-term (12 and 24 months) predictors of SSE among a sample of melanoma survivors. To our knowledge, this is the only study to date to examine long-term predictors of SSE adherence following an educational session on how to effectively conduct SSE to identify melanoma early. The educational session, administered to all of the participants enrolled, was designed to match the best practice protocols delivered in primary care for patients with melanoma, who have a much higher risk for subsequent melanoma than the general population.

Contribution of Authors

The four manuscripts included in the present thesis are original research. I am the first author on all of the manuscripts, as I contributed to the conception and design of each paper; conducted the acquisition, analysis, and interpretation of data; completed the first original draft of each paper; incorporated critical feedback from co-authors and reviewers; and prepared the final version of each paper.

The first manuscript is co-authored by Chelsea Moran, Brett Thombs, Alan Geller, Jochen Ernst, Emily Kingsland, and Annett Körner. Dr. Körner contributed to the design of the study, gave feedback and revised the first draft, revised and approved the final draft. Ms. Moran contributed to the study selection and data extraction (as reviewer 2), gave feedback on several drafts, read and approved the final draft. Drs. Thombs, Ernst, and Geller contributed critical feedback to earlier drafts of the manuscript, reviewed, and approved the final draft of the manuscript. Ms. Kingsland conducted the systematic search, read and approved the final draft. All authors read and approved the final draft of the manuscript.

The second manuscript is co-authored by Chelsea Moran, Catherine Bergeron, Danielle Rice, Brett Thombs, Alan Geller, Emily Kingsland, and Annett Körner. Drs. Körner and Thombs contributed to the design of the study, gave feedback and revised the first draft, revised and approved the final draft. Ms. Moran and Ms. Bergeron contributed to the study selection and data extraction. Ms. Moran, Ms. Bergeron, Ms. Rice, and Drs. Thombs, Geller, and Körner contributed critical feedback to earlier drafts of the manuscript, reviewed, and approved the final draft of the manuscript. Ms. Kingsland conducted the systematic search, read and approved the final draft. All authors read and approved the final draft of the manuscript.

The third manuscript is co-authored by Chelsea Moran, Catherine Bergeron, Martin Drapeau, Alan Geller, Abbas Kezouh, Gerald Batist, and Annett Körner. Dr. Körner contributed to the design of the study, gave feedback and revised the first and subsequent drafts, revised and approved the final draft. Ms. Moran and Dr. Abbas Kezouh contributed to data analysis. Ms. Moran and Ms. Bergeron assisted with writing the method section, formatted the tables, and edited the references. Drs. Geller, Batist, Drapeau, and Ms. Moran

contributed critical feedback to earlier drafts of the manuscript, reviewed, and approved the final draft of the manuscript. All authors read and approved the final draft of the manuscript.

Background and Rationale

Literature Review

Skin cancers are the most commonly diagnosed cancers in Canada and the United States (Erdei & Torres, 2010; Linos, Swetter, Cockburn, Colditz, & Clarke, 2009; Rogers, Weinstock, Feldman, & Coldiron, 2015). Melanoma, which is the most lethal type of skin cancer, is the 7th most commonly diagnosed cancer in Canada (Canadian Cancer Statistics, 2015). While melanoma accounts for only for 4% of all skin cancer diagnoses, it is responsible for 80% of deaths from skin cancer (Krueger & Williams, 2010). It is the most common cancer in women aged 25-29, second only to breast cancer in women 30-34 years old and 60% of all melanomas occur before the age of 65 years (Bleyer, O'Leary, Barr, & Ries, 2006; de Vries, Bray, Coebergh, & Parkin, 2003; Hausauer, Swetter, Cockburn, & Clarke, 2011; Horner et al., 2009; Ries et al., 2000). In North America, the incidence of melanoma has doubled in the last decades. In Canada, of the total numbers of new cancer cases in 2015 (100,00 males, 96, 400 females), 3.6 % in males and 3.2 % in females were melanomas. Also, in 2015 there were 6800 new cases and 1150 deaths from melanoma compared to 2400 new cases and 500 deaths in 1989 (Canadian Cancer Statistics, 2015). Data from the US suggest that in 2018, there will be 91,270 new cases and 9,320 deaths from melanoma in the US (Howlader et al., 2016).

Exposure to ultraviolet light (UV) is generally accepted as the major cause of melanoma. As UV light exposure is a modifiable risk factor for melanoma, starting in the early 1970's public health campaigns started to promote sun protection. The top public health endorsed strategies targeting primary prevention of melanoma include sun protection and reduced bed tanning and sun lamps usage (Canadian Cancer Statistics, 2015). Non-modifiable risk factors for melanoma include a personal history of melanoma, which is associated with a life-long elevated risk for developing subsequent melanomas (Burdern et al., 1994; Geller, Swetter, Brooks, Demierre, & Yaroch, 2007; Uliasz & Lebwohl, 2007); being a first-degree relative of a melanoma patient (Gandini, Sera, Cattaruzza, Pasquini, Zanetti, et al., 2005); having an specific genetic mutation (e.g., MC1R and CDKN2A) (Fargnoli, Gandini, Peris, Maisonneuve, & Raimondi, 2010); being a childhood survivor of a cancer

treated with radiation (Friedman et al., 2010); having a compromised (supressed) immune system, such as after a transplant (Hollenbeak et al., 2005); having more than 100 nevi or more than 5 atypical nevi (Gandini, Sera, Cattaruzza, Pasquini, Abeni, et al., 2005); or having certain phenotypic features, such as light hair color, blue eyes, freckled and/or easily burned skin (Gandini, Sera, Cattaruzza, Pasquini, Zanetti, et al., 2005). These groups of individuals have a higher risk to develop melanoma compared to the general population.

Melanoma tumours grow faster than other skin cancer tumours and can metastasize when they are only 1 mm in depth (Safarians, Sternlight, Freiman, Huaman, & Barsky, 1996; Yang et al., 2009). Tumour thickness at diagnosis is the best predictor of survival, with thicknesses of < 1 mm being associated with highest survival (Baade et al., 2006; Balch et al., 2009; Balch et al., 2001; Eisemann et al., 2012; Green, Baade, Coory, Aitken, & Smithers, 2012). The 5-year survival rate is excellent at 98.4% for patients diagnosed with localized, early stage disease (stage 1); however, survival is much lower at 22.5% for distant, advanced stage disease (stage 3-4) (Howlader et al., 2016). There is consensus within the clinical and scientific communities that establishing an early diagnosis in a pre-metastatic phase of tumour development (i.e., secondary prevention) must be the overarching goal of interventions designed to reduce melanoma-related mortality (Garbe et al., 2003; Markovic et al., 2007; Weinstock, 2006). Further, intervention strategies have the greatest impact if they focus on early detection of melanoma amongst those who are at greatest risk of developing the disease (Geller et al., 2007) such as individuals with one or more risk factors.

Given that melanoma is visually recognizable and highly curable when detected in early stages, but increasingly therapy-resistant and potentially lethal as the tumour progresses (Markovic et al., 2007), the most significant impact on mortality reduction is attributed to secondary prevention, which entails the early detection and timely removal of melanoma (Berwick et al., 2005; Cokkinides et al., 2006; Gandini, Sera, Cattaruzza, Pasquini, Picconi, et al., 2005; Geller et al., 2007; Kennedy, Bajdik, Willemze, De Gruijl, & Bouwes-Bavinck, 2003). Early detection (or secondary prevention) of melanoma is achieved through physician-led skin examination and skin self-examination. The most common visual inspection technique used for the identification of melanoma is the ABCDE criteria (Abbasi, Shaw, Rigel, & et al., 2004; Friedman et al., 1985),

which identifies problematic lesions on account of Asymmetry, irregular Borders, varying shades and Colours inside one mole, large Diameter (> 6 mm), and the Evolution or changing of these parameters.

Empirical studies have consistently shown an association between the skin exam administered by trained physicians and thinner (i.e., earlier stage) melanoma tumours at diagnosis, when compared to no skin exams (Aitken, Elwood, Baade, Youl, & English, 2010) or self-administered skin exams (De Giorgi et al., 2012; Pollitt et al., 2009; Swetter, Pollitt, Johnson, Brooks, & Geller, 2012). In addition, a large population-based case control study (78% of all eligible melanoma cases diagnosed between 2000 and 2003 in Queensland, Australia N=3762 and N=3824 controls) found that physician-led clinical skin exam (CSE) three years prior to diagnosis was associated with a 14% lower risk of a thick (i.e., advanced) melanoma at diagnosis (Aitken et al., 2010). Relying entirely on the clinical skin exam to diagnose melanoma early, however, is not a realistic strategy for the majority of individuals living in North America, since less than 20% of adults receive annual preventive health check-ups (Mehrotra, Zaslavsky, & Ayanian, 2007). As such, various melanoma prevention communities, including individual experts, prevention and advocacy agencies (e.g., American Academy of Dermatology, Canadian Cancer Society, Cancer Care Ontario in Canada, Melanoma Network of Canada), and national policy makers (Macbeth, Newton-Bishop, O'Connell, & Hawkins, 2015; National Collaborating Centre for Cancer, 2015) recommend that at-risk individuals should be advised to a) perform skin self-exams (or SSE) in between medical check-ups and b) seek medical attention when problematic lesions are identified.

There is in fact empirical evidence for the benefits of SSE practice by individuals at risk for melanoma. Cross-sectional research found that patients and family members detected up to 50-80% of all melanomas (Carli, De Giorgi, Betti, et al., 2003; De Giorgi et al., 2012; Swetter et al., 2012). Also, increased thoroughness of the skin self-exam (or extent of skin covered) was associated with thinner lesions at diagnosis (Pollitt et al., 2009); patients who examined at least some parts of their body had thinner lesions at diagnosis compared to those who did not examine their skin (Carli, De Giorgi, Betti, et al., 2003; Pollitt et al., 2009); and individuals who conducted SSE were twice as likely to self-detect melanoma and less likely to have thick (advanced) tumours at diagnosis compared to those who did not practice SSE (Titus et al., 2013).

Even though cutaneous melanomas are readily visible on the skin surface and it is well-known that SSEs are related to better prognosis (Aitken et al., 2006; Geller et al., 2004; Koh, 1992; Robinson, Fisher, & Turrisi, 2002; Terushkin & Halpern, 2009), many individuals at an increased risk do not perform systematic skin exams regularly (Berwick, Begg, Fine, Roush, & Barnhill, 1996; Carli, De Giorgi, Palli, et al., 2003; Manne & Lessin, 2006; Mujumdar et al., 2009). Reported SSE rates among individuals at high risk vary from 16% (monthly SSE) (Glenn, Chen, Chang, Lin, & Bastani, 2016) to 57% (last 3 years) (Olsen et al., 2015) depending on the method of assessing SSE.

Research studies investigating barriers and facilitators of SSE among high-risk groups identified several un-modifiable, i.e., personal or family history, female sex, higher education (Carli, De Giorgi, Palli, et al., 2003; Glenn et al., 2016; Manne & Lessin, 2006; Olsen et al., 2015) and modifiable characteristics, i.e., greater knowledge about melanoma (Robinson et al., 2002), higher perceived susceptibility to melanoma (Glenn et al., 2016; Olsen et al., 2015; Robinson et al., 2002), positive attitude towards SSE (Robinson et al., 2002; Robinson, Turrisi, & Stapleton, 2007), confidence in being able to perform an efficacious skin self-exam (Azzarello et al., 2006; Friedman et al., 1991; Robinson et al., 2002; Robinson et al., 2007), and having a physician recommend SSE (Chiu, Won, Malik, & Weinstock, 2006; Manne & Lessin, 2006; Robinson, Rigel, & Amonette, 1998; Robinson et al., 2007). In addition, several studies have shown that SSE behavior can be improved with educational interventions that focused on teaching people how to check their own skin for problematic lesions (Oliveria et al., 2004; Manne et al, 2010; Turrisi et al., 2015). However, there are several known limitations to the literature exploring predictors of SSE, which include the lack of a standardized operationalization of SSE, which directly affects the reported rates of this behaviour; the limited inclusion of psychosocial variables, such as distress, coping strategies and physician support, as only a few studies addressed these latter constructs in relation to SSE; and quite limited duration of follow-up assessments (mainly 3-4 months), which affects the generalizability of findings from such studies, given that adherence to health behaviours decreases over time (DiMatteo, Giordani, Lepper, & Croghan, 2002; Glanz, Lewis, & Rimer, 2008).

In sum, there's a strong argument from the empirical literature that the early detection of melanoma is associated with less advanced disease and potentially lower melanoma-related mortality. While most melanomas are detected by patients, spouses, and other family members, physician-detected cancerous lesions tend to be thinner, representing an earlier disease stage, than self-detected lesions. Self-examination conducted in tandem with the clinical exam appears to be a desirable and feasible approach to the early detection of melanoma. Despite SSE being an integral part of clinical guidelines for the secondary prevention (early detection) of melanoma among high-risk groups, many individuals at risk do not practice SSE regularly or thoroughly. Studies, including randomized controlled trials, have shown that rates of SSE can be improved through patient education, but their overall effect has not been systematically assessed. Further, little is known about those who adhere to SSE clinical recommendations (e.g., for SSE) versus those who do not, especially in the long-term. Acquiring knowledge on the effectiveness of interventions focused on improving SSE in at-risk individuals and identifying the strongest short- and long-term predictors of SSE behaviour will enable researchers and clinicians to design intervention protocols targeting core issues in melanoma prevention, and, thus, contribute to improved quality of life for patients, decreased need for invasive treatments, and ideally improved survival.

Research Objectives

The aim of this research is three-fold: a) to investigate how SSE is assessed in clinical trials with populations at increased risk for melanoma, b) to evaluate the effect of behavioral interventions targeting SSE in at-risk populations and c) to identify the short- and long-term predictors of SSE in a sample of at-risk individuals. More specifically, manuscript 1 of the dissertation is an evaluation of how SSE is defined and measured in randomized controlled trials testing behavioural interventions among individuals at increased risk for melanoma. Manuscript 2 is a systematic review of randomized controlled trials evaluating the effect of behavioral interventions targeting SSE in at-risk populations on melanoma-related mortality, early detection of melanoma, and melanoma preventive behaviours (e.g., SSE). Manuscript 3 is a longitudinal investigation of

predictors of SSE behavior in a sample of patients who are at risk for subsequent skin cancers due to a personal history of melanoma.

Manuscript 1: Assessment of Skin Self-Examination Among Individuals at Increased Risk for Melanoma: A Systematic Review of Randomized Controlled Trials

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Conflict of Interest

None of the authors declare any conflict of interest. Alan C. Geller was the senior author of the Geller et al., 2006 trial, which is one of the trials included in this review.

Authors' Contribution:

AC, BT, AK Designed the study.

AC, CM Conducted study selection and data extraction.

AC conducted the data synthesis and completed the first draft of the manuscript.

CM, BT, AG, JE, AK Contributed critical feedback to earlier drafts for the manuscript, reviewed, and approved the final draft of the manuscript.

EK conducted the systematic search, reviewed, and approved the final draft of the manuscript.

All authors read and approved the final draft of the manuscript.

Abstract

Background

Currently there is no standardized method to assess skin self-examination as a patient-reported outcome, which affects the interpretation, comparison, and synthesis of findings from different empirical studies. The aim of the current study was to investigate how SSE behaviour was defined (as per instructions given to participants) and assessed in randomized controlled trials (RCTs) involving behavioural interventions with individuals at increased risk for melanoma.

Methods

Data sources included MEDLINE, PsycINFO, EMBASE, CINAHL, Web of Science, the Cochrane Central Register of Controlled Trials, Proquest Dissertations and Theses and Conference Proceedings, and trial registries, searched from inception through February 17, 2017. Articles in any language were included if they reported on RCTs of behavioural interventions for individuals at increased risk for melanoma, which used SSE as an outcome. Two reviewers carried out the selection of relevant trials and conducted data extraction and quality assessment. The systematic review was registered with the International Prospective Register of Systematic Reviews (CRD42016033765).

Results

The review identified 12 unique trials. Participants in all of the trials were instructed to perform SSE, but only 6 trials reported what SSE entailed, such as periodic checking of the skin, use of mirrors or another person for inaccessible body areas, and use of the ABCDE criteria to identify problematic lesions. SSE behaviour was assessed via single items inquiring about skin self-exams (SSE) (11 trials), items inquiring about partner-assisted skin exams (PASE) (6 trials), and items inquiring about conducting skin exams with tracking or monitoring devices such as body maps, generic melanoma pictures, melanoma detection guidelines, or personal whole-body photographs (4 trials). There was substantial variability in how SSE behaviour was assessed across trials, including how the items were phrased (SSE behaviour performed or not; frequency of SSE; SSE counts; or recency of last SSE), the number of items used (range 1-17), the response formats used (different ranges used

when SSE was scored as a continuous variable), and the methods used for scoring the items (as binary or continuous). Beyond face validity, there was no evidence for other types of validity or reliability for the items used to assess SSE behaviour.

Conclusions

Given that SSE assessment is largely inconsistent and there is no evidence supporting the validity of the SSE items used in melanoma prevention trials, future research is needed to investigate the measurement properties of SSE assessment tools. This will improve the interpretability and comparability of the empirical results in this prevention research domain and ameliorate the synthesis of findings across trials.

Assessment of Skin Self-Examination Among Individuals at Increased Risk for Melanoma: A Systematic Review of Randomized Controlled Trials

Skin cancers are the most frequently diagnosed cancers in the United States and Canada (Rogers, Weinstock, Feldman, & Coldiron, 2015). Melanoma is the most lethal type of skin cancers (American Cancer Society, 2016; National Center for Health Statistics, 2011; National Cancer Institute, 2011), as it grows and spreads faster than non-melanoma skin cancers (Safarians, Sternlight, Freiman, Huaman, & Barsky, 1996; Yang et al., 2009). Several populations have a substantially increased risk for melanoma compared to the general population, such as individuals with a personal history of melanoma (Youlden, Youl, Soyer, Aitken, & Baade, 2014), first-degree relatives of melanoma patients (Gandini, Sera, Cattaruzza, Pasquini, Zanetti, et al., 2005), individuals with specific genetic mutations (e.g., MC1R and CDKN2A) (Fargnoli, Gandini, Peris, Maisonneuve, & Raimondi, 2010), childhood survivors or cancer treated with radiation (Friedman et al., 2010), immuno-suppressed individuals, such as those undergoing organ transplant procedures (Hollenbeak et al., 2005), individuals with more than 100 nevi or with more than 5 atypical nevi (Gandini, Sera, Cattaruzza, Pasquini, Abeni, et al., 2005), and individuals with certain phenotypic features, such as blond or red hair color and tendency to freckle (Gandini, Sera, Cattaruzza, Pasquini, Zanetti, et al., 2005).

When melanoma is detected early and treated, the survival rates are excellent. In fact, the 5-year relative survival rates for localized (i.e., stages 0-II) disease are 98.4%, compared to 22.5% for distant or metastatic (i.e., stages II-IV) disease (Howlader et al., 2016). Tumour thickness/depth of invasion at diagnosis is the best predictor of survival (Baade et al., 2006; Balch et al., 2009; Eisemann et al., 2012; Green, Baade, Coory, Aitken, & Smithers, 2012). Thus, early detection and timely treatment (surgical excision of the tumour) are crucial to survival. Early detection of melanoma could reduce the psychosocial costs for affected individuals and the financial/economic burden incurred by the required medical treatment and the loss of work time. A diagnosis of metastatic melanoma is emotionally taxing for patients and their families (Dunn, Watson, Aitken, & Hyde, 2016), and substantially more medical resources are allocated to managing metastatic melanoma versus earlier stages (Tsao, Rogers, & Sober, 1998; Guy, Ekwueme, Tangka, & Richardson, 2012). Because most of the

melanomas develop with a visible, pre-clinical phase (i.e., visible changes on the skin) melanomas are amenable to early detection by means of visually inspecting the skin by physicians and lay persons (Friedman, Rigel, & Kopf, 1985; Hamidi, Peng, & Cockburn, 2010; Weinstock, 2000).

Common visual inspection strategies used for melanoma early detection include the ABCDE criteria, the 7-point Glasgow checklist, and the "ugly duckling" method, which have been developed for clinicians and the general public (Tsao et al., 2015). The ABCDE criteria (Abbasi, Shaw, Rigel, & et al., 2004; Friedman et al., 1985) were developed to identify problematic lesions on account of Asymmetry, irregular Borders, varying shades and Colours, large Diameters (> 6 mm), and whether they are Evolving or changing over time. The Glasgow 7-point checklist (MacKie et al., 2007) consists of 7 key features more commonly associated with melanoma than with other skin cancers (sensory change, diameter [≥1 cm], lesion growth, irregular edge, irregular pigmentation, inflammation, and crusting, oozing, or bleeding), further refined (Healsmith, Bourke, Osborne, & Graham-Brown, 1994) to include 3 primary (change in size, shape or color) and 4 secondary features (inflammation, crusting or bleeding, sensory change, and diameter [≥ 7 mm]). The "ugly duckling" (Grob & Bonerandi, 1998) aims to the identify moles or lesions (skin spots) that stand out when compared to rest of the moles present on the skin.

Empirical studies have consistently shown an association between the skin exam administered by trained physicians and thinner (earlier stage) melanoma tumours at diagnosis, when compared to no skin exam (Aitken, Elwood, Baade, Youl, & English, 2010) or self-administered skin exams (De Giorgi et al., 2012; Pollitt et al., 2009; Swetter, Pollitt, Johnson, Brooks, & Geller, 2012). Relying entirely on the clinical skin exam to diagnose melanoma early, however, is not a realistic strategy for the majority of individuals living in North America, where less than 20% of adults receive annual preventive health check-ups (Mehrotra, Zaslavsky, & Ayanian, 2007). In addition, studies have also shown that the vast majority of melanomas (50-80%) are detected by patients and family/friends (Carli et al., 2003; De Giorgi et al., 2012; Swetter et al., 2012). This led the melanoma prevention community, including experts, prevention and advocacy agencies (e.g., American Academy of Dermatology, Canadian Cancer Society, Cancer Care Ontario in Canada), and national policy

makers (Macbeth, Newton-Bishop, O'Connell, & Hawkins, 2015; National Collaborating Centre for Cancer, 2015) to recommend that at-risk individuals be advised to perform skin self-exams (or SSE) and seek medical advice when problematic lesions are detected. However, medical recommendations for how SSE should be performed and how often are not consistent for individuals in similar risk categories (Watts et al., 2015) and do not necessarily map onto specific, well-defined criteria. More specifically, some guidelines state that SSE should be performed without including details about "how" or "how often", others include recommendations that SSE be performed and supplemented occasionally with palpation of the lymph nodes, some provide details about what a typical skin exam entails (e.g., using the ABCDE criteria to identify problematic lesions; using mirrors or asking someone else for help with checking of the back areas), and some simply make references to external resources (e.g., websites) with more information about SSE and skin cancer prevention in general (Watts et al., 2015). For example, the most recent NICE guidelines for melanoma follow-up in the public healthcare system in the UK recommend the delivery of both oral and written instructions on SSE for patients and their families but fail to specify the details of such SSE instructions (NICE, 2015). Guidelines recommend monthly SSE, SSE every 3-6 months, or do not state the time interval (Marciano, Merlin, Bessen, & Street, 2014; Watts et al., 2015). Inconsistent or vague recommendations about SSE can have negative implications for research (e.g., difficulty to assess the impact of adherence to the medical recommendations using meta-analytic procedures) as well as clinical practice (e.g., if clinicians cannot provide concrete recommendations about how SSE should be performed, it would likely negatively impact the implementation and uptake of SSE behaviours by patients). This study will review and summarize the evidence on the operationalization of SSE in randomized controlled trials testing interventions to promote SSE behaviour.

Research Objectives

The objectives of this systematic review were to investigate a) how SSE was defined (conceptualized); b) how SSE was assessed; c) the consistency of methods used to assess SEE; and d) the evidence supporting the validity and reliability of the SSE assessment tools used in behavioural interventions with individuals at increased risk for melanoma.

Method

The research questions addressed in this review pertain to the tertiary objective of a larger systematic review assessing the impact of behavioural interventions with individuals at increased risk for melanoma on skin melanoma-related mortality, melanoma early detection, and melanoma prevention behaviours (e.g., SSE). The systematic review was registered with the International Prospective Register of Systematic Reviews (CRD42016033765).

Search Strategy

The search strategy was developed by a research librarian (EK) in collaboration with the research team and was peer-reviewed by a second librarian. Medline, EMBASE, CINAHL, PsycINFO, Web of Science, and the Cochrane Central Register of Controlled Trials were searched from inception to February 2017. The following trial registries were also searched: Clinicaltrials.gov, UK Clinical Trails Gateway, International Clinical trials Registry Platform Search Portal, and the Australian and New Zealand Clinical Trials Registry. The search strategy (see Appendix 1) was developed for Medline and adapted to the remaining databases. Results from all databases were imported into EndNote, where duplicate removal was performed.

Identification of Eligible Studies

Study design. RCTs. Studies with any other study design were excluded.

Population. Adults (18 years of age or older) at increased risk for developing melanoma, as defined by primary studies (e.g., patients with a personal history of melanoma; first degree relatives of melanoma patients; immunosuppressed individuals; survivors of childhood cancers treated with radiation; individuals with phenotypic features such as freckles, fair skin or hair color, presence of more than 5 nevi). For studies that included a mixed population of eligible and non-eligible individuals, we included the study if the eligible individuals could be differentiated from the non-eligible individuals and if statistics were provided separately for our population of interest. For a detailed list of risk categories and eligibility criteria, please refer to Appendix 2.

The current review focused on populations with an increased risk of melanoma incidence, primarily because the recommendations for the prevention of melanoma, as currently defined by North American clinical practice guidelines, are similar across these groups. We therefore excluded studies with a general population, such as studies conducted with primarily Caucasian populations, who are arguably at higher risk for melanoma than populations of colour, and with Caucasian men > 50 years of age, who are at higher risk of dying from melanoma than any other group. Notably, most intervention studies conducted with the general population and men > 50 years of age were conducted in Australia, which has the highest incidence of melanoma in the world. This review aims to inform public health policy in Canada and the United States, where melanoma incidence is significantly lower than in Australia and the clinical guidelines consistently recommend SSE only for populations at higher risk compared to that of the general population.

Interventions. Eligible interventions included informational (passive delivery of information on prevention/ early detection), behavioural (active demonstration of preventive behaviours/ skills), psychological (delivery of counselling or psychotherapeutic interventions to assist with the adoption of preventive behaviours), and clinical strategies (non-pharmacological/ non-surgical interventions that can only be delivered by medical professionals: GP and dermatologists; clinical skin exams, genetic counselling). Interventions could be delivered in any format (e.g., in person, via pamphlets, via the internet) and administered by professionally trained (e.g., nurses) or non-professionally trained individuals (e.g., research assistants, peers).

Comparison. We included RCTs with any non-active control (e.g., standard of care, treatment as usual, attention control, no treatment) or active control (e.g., another active intervention).

Outcomes. ***SSE conceptualization***. This refers to the conceptual explanation of what a self-exam entails (e.g., checking the skin of specific body parts versus entire body; using help from another person to check hard to see body areas or using mirrors; tracking changes; the optimal/recommended frequency of the skin exam), as described in the trial registration and/or the trial report, specifically the section pertaining to the instructions and recommendations given to participants in the trial.

SSE assessment. This pertains to the instruments used to assess SSE behaviour across trials, including the specific items or scales, the response options, the scoring (how the construct/ variable was used in analyses), and the timeframe of assessment (the time span for which the SSE behaviour was assessed, e.g., "last 2 months" versus "last 12 months").

Consistency of methods used to assess SSE. We investigated whether the SSE assessment methods were comparable across trials.

Reliability and validity of the SSE instruments. The investigation of the validity and reliability of the SSE instruments used in trials was conducted with respect to several domains included in the COSMIN checklist (COSMIN; (Mokkink et al., 2010)) checklist: content validity (or degree to which the content of the instrument accurately reflects the construct that it purports to measure), criterion validity (the degree to which the scores of an instrument adequately reflect a "gold standard" of assessment), and construct validity (the degree to which the scores of an instrument are consistent with hypotheses based on the assumption that the instrument accurately measures a specific construct); internal consistency reliability (the degree of interrelatedness among items) and test-retest reliability.

Study Selection

Two raters (AC, CM) independently reviewed the titles and abstracts of all identified citations using a predetermined coding manual (see Appendix 3) using specialized software for systematic reviews, i.e. Distiller SR (Evidence Partners, 2017). If either one of the raters deemed an abstract as potentially eligible, a full review was undertaken, also done independently by two raters. Disagreements after the full text review were resolved by consensus between the raters, with the possibility of a third team member (AK) to aid with the decision making.

Data Extraction

Two raters (AC, CM) independently extracted and entered data from relevant trials into pre-designed excel spreadsheets. Data extracted included study characteristics (first author's last name, publication year, country of study, funding source, trial registration number, population, type of intervention and control, N

randomized to intervention and control, age and gender descriptive statistics) and data pertaining to the research questions. For outcome 1, definition of SSE, we extracted information about a) the instructions given to patients about how to conduct SSE, b) the recommended frequency of SSE delivered, and c) how the SSE behaviour was defined in the trial report. For outcome 2, SSE assessment, we extracted all of the items used to assess SSE (regardless of whether they were used in the data analysis not), the response options, the time frame of assessment, and the scoring of the SSE variables. For outcome 3, consistency of methods used to assess SSE, we used the same data as extracted for outcome 2 in order to draw conclusions about differences and similarities across trials. For outcome 4, validity and reliability of SSE instruments, we extracted validity and/or reliability data from the trial report and from the additional sources cited in the method sections of the trial reports, identified through manual searching of reference lists. Additional referenced works were deemed relevant for this review if a) the aim of the study was to evaluate the properties of an SSE instrument identical or similar to one used in our included trials and/or b) the study reported results for an SSE instrument (identical or similar to one used in our included trials) in the context of investigating its psychometric properties. Disagreements about data extraction were resolved by consensus, with a third investigator (AK) consulted if necessary.

Data Presentation and Synthesis

Results were presented in tabular form and a narrative synthesis was provided for each research question.

Results

Results of the Search

The PRISMA flow chart reflecting the study selection process was included in Figure 1. The combined search of the databases generated 552 unique citations, of which 459 were excluded after reviewing titles and abstracts and 76 after the full-text review. At both stages, we excluded articles based on the following criteria: a) if the population was not at increased risk compared to the general population, b) if the study did not use an RCT design, and c) if the study did not assess the behavioural outcomes of interest (e.g., SSE). The full text was

reviewed for 93 articles and 12 unique trials (and 5 related trial registrations) were included in this review. Through manual searching of the method sections and reference lists of the trial reports included in this review, we identified 18 additional articles potentially relevant to the validity and/or reliability of the SSE measures used in the trials. Upon screening of the full texts (n=18, included in Appendix 4), none met our a priori validity and/or reliability criteria for inclusion.

Characteristics of the Included Trials

Detailed sample characteristics of the included trials can be found in Table 1. Ten trials were conducted in the United States (Bowen, Burke, Hay, Meischke, & Harris, 2015; Geller et al., 2006; Glanz, Schoenfeld, & Steffen, 2010; Glanz et al., 2015; Glanz et al., 2013; Manne et al., 2010; Oliveria et al., 2004; Robinson, Turrisi, Mallett, Stapleton, & Pion, 2010; Robinson, Turrisi, & Stapleton, 2007; Turrisi, Hultgren, Mallett, Martini, & Robinson, 2015), 1 in the United Kingdom (Glazebrook, Garrud, Avery, Coupland, & Williams, 2006), and 1 in France (Rat et al., 2014). Four trials were conducted with melanoma patients (Bowen, Burke, Hay, Meischke, & Harris, 2015; Robinson, Turrisi, Mallett, Stapleton, & Pion, 2010; Robinson, Turrisi, & Stapleton, 2007a; Turrisi, Hultgren, Mallett, Martini, & Robinson, 2015), 2 trials with first degree relatives of melanoma patients (Geller et al., 2006; Manne et al., 2010), and 6 trials with at-risk individuals recruited in primary care outpatient clinics (Glanz, Schoenfeld, & Steffen, 2010; Glanz et al., 2015; Glanz et al., 2013; Glazebrook et al., 2006; Oliveria et al., 2004; Rat et al., 2014). The minimum number of patients randomized per condition was 19 (Robinson et al., 2010). Only 5 of the 12 trials had been registered with trial registry platforms (Glanz et al., 2015; Manne et al., 2010; Rat et al., 2014; Robinson et al., 2007a; Turrisi et al., 2015). Among the pre-registered trials, only one was registered prior to the commencement (Glanz et al., 2015).

Outcome 1: SSE Conceptualization

Eleven of the 12 trials provided recommendations for SSE behaviours to both intervention and control participants and one trial with a waitlist control design only recommended SSE to participants in the active intervention arm (Bowen et al., 2015). Detailed SSE recommendations were reported in 5 trials (Glanz et al., 2015; Oliveria et al., 2004; Robinson et al., 2010; Robinson et al., 2007a; Turrisi et al., 2015), including periodic

(e.g., monthly) checking of the skin of the entire body, with the help of mirrors or someone else to assist with the checking of hard-to-reach areas; the ABCDE criteria were the recommended strategy for the identification of problematic lesions. Between these 5 trials there were small variations with respect to the tools recommended for monitoring and tracking the skin exams, which included body maps and scorecards (Robinson et al., 2010; Turrisi et al., 2015), whole body photographs (Oliveria et al., 2004) or they were not specified (Glanz et al., 2015; Robinson et al., 2007a). The remaining 7 trials, while also indicating that SSE was recommended, did not report sufficient detail to clearly delineate what the skin exam entailed in the particular studies. With respect to the recommendations as to how often (or how frequently) SSE should be performed, 3 trials reported that participants were encouraged to perform "monthly SSE" (Glanz et al., 2015; Robinson et al., 2010; Turrisi et al., 2015) and 9 trials did not include in the trial report the recommended frequency for SSE.

Outcome 2: Assessment of SSE

The measurement characteristics of the SSE instruments used in the trials are included in Table 2. One trial included a working definition of SSE, i.e. "careful examination of all moles, including those on the back at least one time in the 12 months after completion of the baseline survey" (Geller et al., 2006) while the remaining 11 trials did not provide such a definition. None of the trials used scales to assess SSE behaviour, but only individual items. The items reflected individual self-exams (SSE without the assistance of another person or the use of monitoring/tracking devices: 11/12 trials) (Bowen et al., 2015; Geller et al., 2006; Glanz et al., 2010; Glanz et al., 2015; Glanz et al., 2013; Glazebrook et al., 2006; Manne et al., 2010; Oliveria et al., 2004; Rat et al., 2014; Robinson et al., 2010; Robinson et al., 2007a), partner-assisted skin exams (PASE: 6/12 trials) (Geller et al., 2006; Glazebrook et al., 2006; Rat et al., 2014; Robinson et al., 2010; Robinson et al., 2007a; Turrisi et al., 2015), and skin exams conducted with tracking or monitoring devices such as body maps, generic melanoma pictures, melanoma detection guidelines, or personal whole-body photographs (4/12) (Geller et al., 2006; Rat et al., 2014; Robinson et al., 2010; Robinson et al., 2007a). The number of items used to assess SSE behaviour ranged from 1 item (Glanz et al., 2010; Manne et al., 2010; Oliveria et al., 2004) to 17 items (Turrisi et al., 2015). Half of the trials used binary variables to assess SSE behaviour (% of endorsed behaviour) (Bowen et al., 2015;

Geller et al., 2006; Glanz et al., 2010; Glazebrook et al., 2006; Oliveria et al., 2004; Rat et al., 2014) and the other half used continuous variables (frequency of behaviour). The timeframe for the assessment of SSE behaviour ranged from "last 2 months" (Bowen et al., 2015) to "last 12 months" (Geller et al., 2006; Rat et al., 2014), the most frequently used timeframe being "last 4 months" (Oliveria et al., 2004; Robinson et al., 2010; Robinson et al., 2007a; Turrisi et al., 2015). For the items scored in a binary fashion (percentages), there were differences between how the endorsed event was categorized: 5 of the 6 trials using binary scoring used "at least 1 SSE during [specified timeframe]" (Bowen et al, 2015; Geller et al, 2006; Glanz et al., 2010; Glazebrook et al., 2006; Rat et al., 2014) and one trial used "at least 3 SSE's in the last 4 months" (Oliveria et al., 2004). For the continuously scored outcomes, the answer choices indicated different frequency ranges for SSE across different trials (Glanz et al., 2015; Glanz et al., 2013; Manne et al, 2010; Robinson et al., 2010; Robinson et al., 2007a; Turrisi et al., 2015).

Outcome 3: Consistency of Methods Used to Assess SSE

A few different modalities were used to assess SSE. Specifically, the phrasing of the items reflected 4 possible ways to assess SSE: a) whether SSE was performed, individually (Bowen et al., 2015; Glanz et al., 2010; Glanz et al., 2015; Glanz et al., 2013; Glazebrook et al., 2006; Manne et al., 2010; Rat et al., 2014), with a partner (Geller et al., 2006; Glazebrook et al., 2006; Rat et al., 2014), or with tracking/monitoring (Geller et al., 2006; Rat et al., 2014); b) the comprehensiveness (completeness) of SSE relative to the extent of the skin checked: few body parts (6-7) (Turrisi et al., 2015), many body parts (Bowen et al., 2015; Turrisi et al., 2015), entire body/ all moles (Geller et al., 2006); c) the recency of the last SSE performed (last months versus longer) (Glanz et al., 2015; Glanz et al., 2013); d) the frequency of SSE (how many times or how often was SSE conducted) individually (Oliveria et al., 2004; Robinson et al., 2007a), with a partner (Robinson et al., 2010; Robinson et al., 2007a; Turrisi et al., 2015) or with tracking/monitoring (Robinson et al., 2010; Robinson et al., 2007a). There was wide variation between the trials with respect to the type of scales used, the response format, and the scoring procedures used for SSE measures, with no two trials using the exact same methods.

Outcome 4: Validity and Reliability of SSE Measures

All of the SSE measures (or items) used in the trials included in this review (n = 12) showed face validity: the items appeared to be relevant to the practice of checking the skin for signs of skin cancer and had been previously used in research to assess the practice of skin self-examination. We could not identify any evidence supporting the content (beyond face validity), construct, or criterion validity of the SSE instruments used by the included trials. With respect to reliability, only 1 of the 12 trials reported internal consistency reliability coefficients for the SSE behaviour items (Turrisi et al., 2015).

Discussion

The goals of this review were to synthesize the literature on the measurement of SSE: how SSE behaviour is defined, how SSE is assessed, how consistent the SSE assessment methods are, and the evidence for the validity and reliability of SSE instruments used in educational and psychological interventions with individuals at increased risk for melanoma. We identified 12 unique trials conducted with individuals at increased risk for melanoma (e.g., melanoma patients, siblings of melanoma patients), all of which recommended SSE as a prevention strategy aimed at the early detection of melanoma. Five of the 12 trials reported the specific recommendations provided to participants about how they should perform SSE: checking the entire body, including hard to reach areas or areas not exposed to the sun (by using mirrors or someone else's help) and using the ABCDE criteria to identify problematic lesions, tracking changes in moles, and recording changes. The frequency with which SSE was to be performed, i.e., "monthly", was reported in only 3 trials. At a minimum, an intervention targeting SSE as a melanoma prevention behaviour should address three aspects: a) identify the preventive health behaviour as an important aspect of prevention (*information*), b) explain or teach (demonstrate) how to actually perform a complex behaviour, such as checking the skin for the early signs of melanoma (*behavioural skills*), and c) state how often participants should perform the health behaviour (e.g., monthly, yearly, or every 6 months) (*recommended frequency of behaviour*). Depending on the theoretical models used to explain health behaviour changes, other features (e.g., motivation, attitudes, and/ or barriers to screening) can also be included. These aspects of the educational interventions are important to

state clearly to participants, and mostly likely they were conveyed in the trials we reviewed. However, it is also important to delineate these clearly in the trial reports, as this transparent and complete reporting allows readers to gage whether there was consistency between the behaviours recommended to participants, as part of the active interventions, versus how the recommended behaviours were assessed post intervention.

We found only one trial that reported an a priori operationalization of SSE behaviour. The lack of a pre-specified definition of SSE behaviour can be problematic. First, it is unclear whether this is a trial reporting issue (i.e., trial authors had a working definition of SSE behaviour, but did not include it in the trial registration and/or the trial report/publication); an issue involving the selective reporting of the trial outcomes (i.e., after-the-fact decision, based on trial findings, to only report significant analyses involving certain SSE conceptualizations, but not others); or a more conceptual issue, relating to the fact that currently there is no standardized way to define SSE. Second, the lack of an a priori conceptual definition of SSE behaviour makes it difficult to investigate the validity, particularly the construct validity, of measures used to assess this behaviour.

Overall, there was variation in how SSE behaviour was assessed across trials with no two trials using identical methods. Across the trials included in this review, there was inconsistency at the level of content of the items used to assess SSE, which encompassed varied behaviours, from checking the skin on specific skin areas (e.g., face) individually, with the help of partners, and with other aids such as melanoma pictures and SSE guiding materials to checking the skin of up to 17 body parts or checking only the moles on the entire body. Also, there were inconsistencies with respect to the number of items used to assess SSE, with an increased number of items being indicative of a larger extent of skin being covered by the exam and/or the complexity of the behaviour assessed (e.g., partner assistance, use of written aids); response format (scales and anchors); the time frame of the assessment, and the scoring of the items. The lack of conceptual consistency with respect to SSE is not surprizing given the current absence of empirical studies (randomized or using other designs) investigating whether different modalities of self-examining the skin lead to differential health (e.g., mortality) or health-related (e.g., early detection) outcomes. In addition, the inconsistencies identified in this review may reflect inconsistencies in the recommendations of SSE by clinical guidelines for melanoma prevention and

follow-up care. For example, different guidelines recommend different time intervals for SSE, ranging from monthly (Bichakjian et al., 2011; Marsden et al., 2010) to every 3-6 months (Australian Cancer Network Melanoma Guidelines Revision Working Party, 2008; Institut National du Cancer (INCa) and Haute Autorit e de Sante (HAS), 2012) or simply do not specify the time interval (National Collaborating Centre for Cancer, 2015). Guidelines also differ in how they recommend SSE. This ranges from simply stating that SSE should be recommended to at-risk individuals *to* teaching sessions with live demonstration on how SSE should be performed and verbal recommendations on how often SSE should be performed (Marciano et al., 2014; Watts et al., 2015). Future research will benefit from establishing the most efficacious modality to perform SSE as well as how often SSE should be performed in order to effectively identify problematic lesions.

This review found no evidence supporting the validity and reliability of SSE measures used across trials, beyond face validity and reliability for two measures. In a few instances, we found articles using measures similar or identical to the ones used in three of our included trials (Bowen et al., 2015; Manne et al., 2010; Oliveria et al., 2004), which reported base rates, correlates, and predictors of SSE (Manne et al., 2004; Robinson, Fisher, & Turrisi, 2002; Weinstock et al., 1999; Weinstock et al., 2004). We excluded these additional sources from the current review because the objective of these articles was not to investigate the validity and/or reliability of SSE instruments, but we would like to acknowledge their existence for researchers who might find these resources helpful when trying to gauge the validity of an SSE assessment tool. We have made every effort to identify source articles regarding the psychometric properties of the SSE instruments used in the trials included in this review. However, our search strategy was not built specifically for the purpose of identifying psychometric properties of SSE measures. Nevertheless, given the preparation, rigour, and resources involved in conducting clinical trials, it is reasonable to expect that if valid and reliable SSE measures existed, they would have been used in at least some of these trials and adequate references would have been included in the trial reports.

As can be seen from this review, there is little agreement in the SSE intervention literature with respect to the conceptualization and measurement of SSE. It might seem intuitive that checking the skin on the entire

body while also using external aids (e.g., partners' help or mirrors) for hard-to-see areas and tracking changes on the skin are necessary components of a "thorough" (or comprehensive, complete) skin self-exam (Weinstock et al., 2004). One might further assume that "thorough SSE" should be recommended to individuals with an increased melanoma risk and thus, that the melanoma research community might want to adopt a definition that addresses these aspects of SSE. However, the reality is that the current melanoma prevention literature does not provide sufficient evidence to conclude that one modality of conceptualizing and measuring SSE is more effective than others at predicting health and health-related outcomes. Currently, we don't know a lot about SSE, including 1) what is the most pertinent definition of SSE behaviour? 2) is there a valid and reliable method to assess SSE behaviour? and 3) are some modalities of assessing SSE more effective than others at predicting health outcomes in individuals at increased risk for melanoma? Answers to these questions have important implications because the way SSE is conceptualized affects the reported SSE rates in the literature. For instance, when SSE behaviour was conceptualized as any skin checking (as opposed to none), SSE rates ranged from 46% among the general population (Robinson, Rigel, & Amonette, 1998) to 70% among a population at increased risk for melanoma (Robinson et al., 2002), and between 75-90 % among individuals with a personal history of melanoma (Kasparian et al., 2012). When SSE behaviour was defined as a deliberate and systematic behaviour of checking the skin, reported rates ranged from 12% throughout one's lifetime to 18% during the past two months among an outpatient population without an increased risk for melanoma (Weinstock et al., 2004). Also, the inconsistent conceptualization and measurement of SSE in tandem with a lack of evidence supporting the validity and reliability of existing SSE measures impede the interpretation, comparison, and synthesis of the results from randomized controlled trials using SSE as an outcome.

Limitations and Future Directions for Research

There are some limitations of this review: we included studies with individuals with varying risks of developing melanoma, all of which were higher than the risk of the general population, and we only focused on randomized controlled trials. We excluded studies conducted with the general population and with individuals at increased risk of being diagnosed with advanced melanoma (e.g., men over the age of 50) as well as studies

with any other research design (e.g., observational) beside RCT. Our population criteria align with most melanoma care guidelines, which recommend SSE only for at-risk individuals (for reviews of guidelines for at-risk individuals, see (Marciano et al., 2014; Watts et al., 2015)). Given our strict inclusion criteria, it is possible that we did not capture all of the existing SSE measures used in melanoma research. Our inclusion criteria, however, was guided by our primary research question, which was to investigate the effect of behavioural interventions on mortality, melanoma early detection, and SSE uptake in high-risk populations. While we may not have identified all of the existing SSE measures, it seems reasonable to assume that we reviewed a representative sample of SSE measures that have undergone a more stringent measure development as they served as outcome variables in resource-intensive randomized controlled trials.

Since we registered our review, we became aware of a 2016 systematic review of melanoma preventive interventions among paediatric and adult populations with a personal or family history of melanoma, which used different inclusion criteria with respect to population and study design (Wu et al., 2016). Our review included several populations at increased risk for melanoma (e.g., individuals with a personal and familial history of melanoma, individuals with phenotypic features, immune-compromised individuals, which all have similarly higher risk of developing melanoma compared to the general population) whereas Wu and colleagues included only individuals with a personal and/or familial history of melanoma. Further, our review only included RCT's whereas Wu and colleagues included other study designs. As a result of applying different inclusion/exclusion criteria, our review included 7 trials, which were not captured by Wu (Wu et al., 2016). Similarly, Wu review included 3 studies with non-RCT designs, which were not captured by our review. Further, their review findings regarding the effectiveness of SSE interventions are difficult to interpret because they did not provide information about how SSE was assessed by the studies included in their review, and rather refer to frequency and thoroughness of SSE interchangeably. Another review published in 2018 (Henrikson et al., 2018) evaluated the effect of randomized and non-randomized clinical trials on several outcomes relevant for melanoma prevention, including SSE. This review included any populations, not just those at high risk, and restricted the interventions to those amenable to primary care settings.

Future studies should examine the construct validity of SSE measures by conducting Delphi investigations involving melanoma prevention experts, researchers and methodologists to reach consensus on the most relevant items to be included in such a measure. Second, it would be important for future studies to investigate the predictive validity of SSE measures. It would be important to establish whether deliberate checking of the skin of the entire body (or of moles pointed out by health care professionals as needing surveillance) differs from casually checking the skin, and whether the use of tracking devices adds a substantial benefit with respect to short and long-term outcomes, such as SSE uptake and melanoma early detection. Such research projects could answer questions about the optimal frequency of SSE behaviour, which could then be incorporated into guidelines of care for individuals at increased risk for melanoma, which is much needed given that the current guidelines recommendations for SSE are mostly consensus-based (Marciano et al., 2014). Ultimately, agreement upon SSE definition (conceptualization) and assessment among the melanoma scholarly community could lay the groundwork for studies testing the impact of SSE behaviour on the early detection of melanoma and melanoma-related mortality.

Conclusion

The current review of behavioural interventions for individuals at increased risk for melanoma found that the outcome measure, skin self-examination (or SSE), is defined and assessed inconsistently across trials. Further, there is minimal evidence supporting the validity and reliability of SSE measures used in behavioural trials for at-risk populations, which compromises the legitimacy of research conclusions. Future research is needed to investigate the psychometric properties of SSE measures, which would be beneficial for studies examining the impact of SSE on health outcomes in populations at increased risk for melanoma.

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Table 1. Characteristics of Trials of Behavioural Interventions with Individuals at Increased Risk for Melanoma

First author, year Country	Funding source Trial registration,acronym	Population	Intervention vs. control	N Randomized	Age M ± SDor n (%)	Female n (%)
1. Bowen, 2015, United States (Bowen et al., 2015)	NIH# P20 HG007243 NCI# R01 CA107430 Unregistered trial Suntalk Study	Melanoma patients	Web-based communication and support vs. Wait-list	Intx 157 Ctrl 156	Total: 56.11 ± 12.33	Total 175 (56)
2. Geller, 2006, United States (Geller et al., 2006)	NCI# R01CA76333 Unregistered trial	FDR (siblings) of melanoma patients	Tailored phone counselling vs. TAU	Intx 237 Ctrl 257	Reported > 51 Intx 105 (44.3) Ctrl 101 (39.4)	Intx 123 (51.9) Ctrl 141 (54.9)
3. Glanz, 2010, United States (Glanz et al., 2010)	NCI #CA 76419 Unregistered trial Project SCAPE	At-risk outpatients (identified with BRAT)	Tailored intervention vs. TAU	Intx 362 Ctrl 362	Intx 42.1 ± 10.8 Ctrl 41.2 ± 11.2	Intx 285 (78.7) Ctrl 276 (76.2)
4. Glanz, 2013, United States (Glanz et al., 2013)	NIH# 5UC2CA148310-02 Unregistered trial GenoMEL Cohort	At-risk outpatients (melanoma patients or FDR)	Genetic counselling vs. TAU	Intx 35 Ctrl 38	Intx 62.4 ± 14.6 Ctrl 56.9 ± 16.1	Intx 28 (80.0) Ctrl 22 (57.9)
5.Glanz, 2015, United States (Glanz et al., 2015)	NIH# 5UC2 CA148310 NCT01356771 PennSCAPE trial	At-risk outpatients (identified with BRAT)	Tailored mailing vs. Generic mailing	Intx 95 Ctrl 111	Completers: Intx 53.5 ± 14.4 Ctrl 56.5 ± 15.7	Completers: Intx 62 (74.7) Ctrl 79 (72.5)
6. Glazebrook, 2006, United Kingdom (Glazebrook et al., 2006)	Trent NHS Unregistered trial Skinsafe trial	At-risk outpatients (family or personal history, phenotypic features, skin type, and number of nevi)	Health education via computer program vs. TAU	Intx 259 Ctrl 330	Intx 38.2 ± 14.3 Ctrl 38.4 ± 15.2	Intx 214 (82.6) Ctrl 259 (78.5)
7. Manne, 2010, United States (S. Manne et al., 2010)	No funding reported NCT00816374	FDR of melanoma patients	Tailored print and counseling vs. Generic print and counselling	Intx 225 Ctrl 218	Intx 48.1 ± 12.6 Ctrl 47.1± 13.9	Intx 135 (60.0) Ctrl 144 (66.1)

First author, year Country	Funding source Trial registration,acronym	Population	Intervention vs. control	N Randomized	Age M ± SDor n (%)	Female n (%)
8. Oliveria, 2004, United States (Oliveria et al., 2004)	No funding reported Unregistered trial	At-risk outpatients (>=5 clinical dysplastic or atypical nevi)	Teaching with photo-book vs. Teaching without photo-book	Intx 49 Ctrl 51	Intx 40.3 ± 10.9 Ctrl 39.4 ± 11.5	Intx 29 (59.2) Ctrl 34 (66.7)
9. Rat, 2014, France (Rat et al., 2014)	No funding reported NCT01610531 "COPARIME project"	At-risk outpatients (identified with SAMScore)	Targeted screening and education vs. TAU	Intx 97 Ctrl 76	Intx 43.6 ± 17.1 Ctrl 42.8 ± 14.6	Intx: 74 (76.0) Ctrl: 58 (76.0)
10.Robinson, 2007, United States (Robinson et al., 2007a)	NCI# 5R21 CA-103833-02 NCT01013844	Melanoma patients	Dyadic learning vs. Solo-learning	Intx 65 Ctrl 65	(Median) Intx 40-49 Ctrl 50-59	Intx: 33 (51.0) Ctrl: 32 (49.0)
11. Robinson, 2010, United States (Robinson et al., 2010)	No funding reported Unregistered, but declared as Pilot for Turrisi trial	Melanoma patients	Intervention via workbook vs. In-person intervention	Intx 21 Ctrl 19	(Median) Intx 40-49 Control 40-49	Intx: 10 (53.0) Ctrl: 11 (52.0)
12.Turrisi, 2015, United States (Turrisi et al., 2015)	NCI# R01 CA154908 NCT01432860	Melanoma patients	In-person intervention vs. Intervention via workbook vs. Intervention via e-Tablet vs. TAU	In-person 165 Workbook 159 Tablet 71 Ctrl 99	(Median) In-person 50-59 Workbook 50-59 Tablet 50-59 Ctrl 50-59	In person 75 (45.5) Workbook 81 (50.9) Tablet 37 (52.1) Ctrl 60 (60.6)

Note. NIH = National Institutes of Health; NCI = National Cancer Institute; FDR = first degree relative; SSE = skin self-examination; TAU = treatment-as-usual; BRAT=Brief skin cancer risk assessment tool; SAMScore = the Self-Assessment Melanoma Risk Score; Intx = intervention; Ctrl = control

Table 2. Operationalization and Measurement of SSE across Trials of Behavioural Interventions with Individuals at Increased Risk for Melanoma

First author, year	Instructions* for SSE	Frequency* of SSE	SSE Assessment				SSE outcomes, as per trial analyses
			Items	Response options	Time frame	Scoring	
1. Bowen, 2015 (Bowen et al., 2015)	Details not reported. Online materials on SSE included in intx.	Not reported	1-7. Did you carefully examine … [7 skin areas] [a] (SSE of specific body parts)	Never Once or more	Last 2 months	Binary (%)	SSE of specific areas At least 1x SSE [body part] in the last 2 months
			8. Did you do a thorough skin examination? (Thorough SSE)	Yes No			SSE At least 1x thorough SSE in the last 2 months
2. Geller, 2006 (Geller et al., 2006)	Details not reported. Materials tailored to individual SSE behaviours included in intx.	Not reported	1. [Have you] carefully examined all of your moles, including those on the back? (SSE by checking all moles)	Yes No	Last 12 months	Binary (%)	SSE At least 1x SSE (checking all moles) in the last 12 months
			2. [Have you] compared all of your moles to see if one stands out? (SSE by comparing all moles)				SSE w/ mole comparison At least 1x SSE (comparing all moles) in the last 12 months
			3. [Have you] asked a family member/ friend to look at your moles? (PASE)				PASE At least 1x PASE in the last 12 months
			4. [Have you] used a picture of moles to help you look? (SSE with picture)				SSE w/ picture At least 1x SSE (using pic to compare moles) in the last 12 months
3. Glanz, 2010 (Glanz et al., 2010)	Details not reported. Written instructions on SSE using ABCDE criteria included in intx and ABCDE bookmark included in ctrl.	Not reported	1. Have you ever/ in the last 3 months conducted a thorough SSE? (Lifetime/ Thorough SSE)	Yes No	Last 3 months	Binary (%)	SSE At least 1x SSE in the last 3 months

First author, year	Instructions* for SSE	Frequency* of SSE	SSE Assessment				SSE outcomes, as per trial analyses
			Items	Response options	Time frame	Scoring	
4. Glanz, 2013 (Glanz et al., 2013)	Details not reported. Generic prevention pamphlet included in intx and ctrl.	Not reported	1. Do you ever closely examine yourself for signs of skin cancer, including melanoma? (Lifetime SSE)	Yes No	Ever	Binary (%)	Not reported
			2. If yes, when did you last examine your skin? (SSE Recency)	1= In the last month 2, 3 = Not reported 4 = Never	Range ("never" to "last month")	Continuous (M/SD)	SSE Recency of last thorough SSE ("never" to "last month")
5. Glanz, 2015 (Glanz et al., 2015)	Instructions on how to perform SSE using ABCDE criteria; how to use mirrors for back areas and scalp; how to track changes in moles included in intx and ctrl.	Monthly SSE	1. Have you ever closely examined yourself skin for signs of skin cancer, including melanoma? (Lifetime SSE) 2. If so, how recently? (SSE Recency)	Items combined: 1 = Never 2 = > 3 months ago 3 = 1-3 months ago 4 = In the last month	Range ("never" to "last month")	Continuous (M/SD)	SSE Recency of last SSE ("never" to "last month")
6. Glazebrook, 2006 (Glazebrook et al., 2006)	Details not reported. Online materials on how to check skin for suspicious lesions included in intx.	Not reported	1. [Have participants been] "checking moles"? (SSE by checking moles) 2. [Have the participants performed] SSE? (SSE, no specifics) 3. [Have the participants] had their skin checked by someone else? (PASE)	Yes No	Last 6 months	Binary (%)	SSE At least 1x SSE in the last 6 months PASE At least 1x PASE in the last 6 months

First author, year	Instructions* for SSE	Frequency* of SSE	SSE Assessment				SSE outcomes, as per trial analyses
			Items	Response options	Time frame	Scoring	
7. Manne, 2010 (Manne et al., 2010)	Details not reported. Instructions on how to perform SSE using ABCDE criteria included in intx and ctrl.	Not reported	1. How often have [participants] examined their skin deliberately and purposefully in the past year/ last 3 months? (SSE by checking skin deliberately and purposefully)	Not reported	Last 3 months	Continuous (M/SD)	SSE Frequency of SSE in the last 3 months
8. Oliveria, 2004 (Oliveria et al., 2004)	Generic video on SSE how-to (systematic checking of skin on the entire body) and nurse-led demo on SSE (systematic checking of entire body using ABCDE criteria to identify problematic lesions) included in intx and ctrl. Individual, whole-body photographs (to track changes) included in intx.	Not reported	1. How many times in the past 4 months did you (or someone else) usually, thoroughly examine your skin? By thorough we mean actually looking at different areas of your skin deliberately and systematically. (SSE Thorough)	Not reported	Last 4 months	Binary (%) 1 = ≥ 3 times 0 = < 3 times	SSE At least 3x SSE in the last 4 months
9. Rat (Rat et al., 2014)	Details not reported. Generic prevention pamphlet included in intx and freely available to ctrl.	Not reported	1. In the last 12 months, did you perform a skin self-examination?" (SSE, no specifics) 2. If yes, did you have assistance from another person or mirror?" (PASE) 3. If yes, did you take a photograph?" (SSE with own photograph)	Yes No	Last 12 months	Binary (%)	SSE At least 1x SSE in the last 12 months PASE At least 1x PASE in the last 12 months SSE w/ own photograph At least 1x SSE w/ photographs in the last 12 months
10. Robinson, 2007 (Robinson et al., 2007a)	Card with ABCDE criteria and SSE RA-led demo*** of SSE how-to (e.g., using magnifying	Not reported	1. [How many] times patients examined their skin? (SSE by checking skin)	0 = Never 1 = Once in last month	Last 4 months	Continuous (M/SD)	SSE Frequency of SSE in the last 4 months ("never" to "daily")

First author, year	Instructions* for SSE	Frequency* of SSE	SSE Assessment				SSE outcomes, as per trial analyses
			Items	Response options	Time frame	Scoring	
	glass for criterium E) included in intx and ctrl.		2. [How many] times patients examined their skin with a partner? (PASE) 3. [How many] times patients reviewed SSE guidelines? (SSE with clinical guidelines) 4. […use of the] Body Map? (SSE with body map)	2 = 2-3 times in last month 3 = Weekly 4 = Daily 0 = Never 1 = Once 2 = 2 times 3 = 3 times	Last 3 months		PASE Frequency of PASE in the last 4 months ("never" to "daily") SSE w/ guidelines Frequency of SSE in the last 4 months ("never" to "daily") SSE w/ body maps Frequency of SSE in the last 4 months ("never" to "daily")
11. Robinson, 2010 (Robinson et al., 2010)	Self-screening kit (ruler, ABCDE card, magnifying glass, body map) and instructions on how to use it included in intx and ctrl.	Monthly SSE	1. How often does the participant perform SSE with a partner? (PASE) 2. How often [does the participant] review skin examination guidelines? (SSE with clinical guidelines)	0 = Never 1 = Once in last month 2 = 2-3 times in last month 3 = Weekly 4 = Daily	Last 4 months	Continuous (M/SD)	PASE Frequency of PASE in the last 4 months ("never" to "daily") SSE w/ guidelines Frequency of SSE in the last 4 months ("never" to "daily")
12. Turrisi, 2015 (Turrisi et al., 2015)	ABCDE criteria explained and self-screening kit (lighted magnifying lens, laminated ABCDE card, body map, and scorecards to track monthly SSE) included in intx and ctrl.	Monthly SSE	(1-17) How often have [the participants] examined … [17 different skin areas] [b] with their partner? (PASE of specific body parts)	0 = 0 times 1, 2, 3 = Not reported 4 = 4 times or more	Last 4 months	Continuous (M/SD) [b, c, d]	PASE Frequency of PASE in the last 4 months ("never" to "daily")

Note. SSE = skin self-examination; PASE = partner-assisted SSE

* Instructions about how to perform SSE and with what frequency, as provided in the trials.

** Recommended frequency of SSE, as part of the interventions tested in the included trials.

*** Trained RA presented the ABCDE info on the card; showed 2 additional color printed examples of E (evolution) of pigmented lesions in 1 year; answered questions about the card content; gave a skills demonstration using a magnifying lens to look at moles; and pointed out irregular borders and uneven colors.

[a] Bowen, 2015 (Bowen et al., 2015): 7 items corresponding to 7 body areas (the front of you from waist up, the front of your thighs and legs, the bottom of your feet, your calves, the back of thighs and legs, the buttocks and lower part of your back, your upper back). [b] Total body SSE α = .96-.98; Total body SSE = 17 items corresponding to 17 different body areas (e.g., front and back of neck; top and soles of feet; front and back of thighs; groin). [c] SSE of easy to see areas α = 0.95-0.98; SSE of easy to see areas = 7 items corresponding to 7 body areas (face, front torso, neck, both hands, arms, legs, and feet). [d] SSE of difficult to see areas α = 0.88-0.95; SSE of difficult to see areas = 6 items corresponding to 7 body areas (scalp, buttocks, back of ears, neck, shoulders, thighs).

PRISMA FLOWCHART

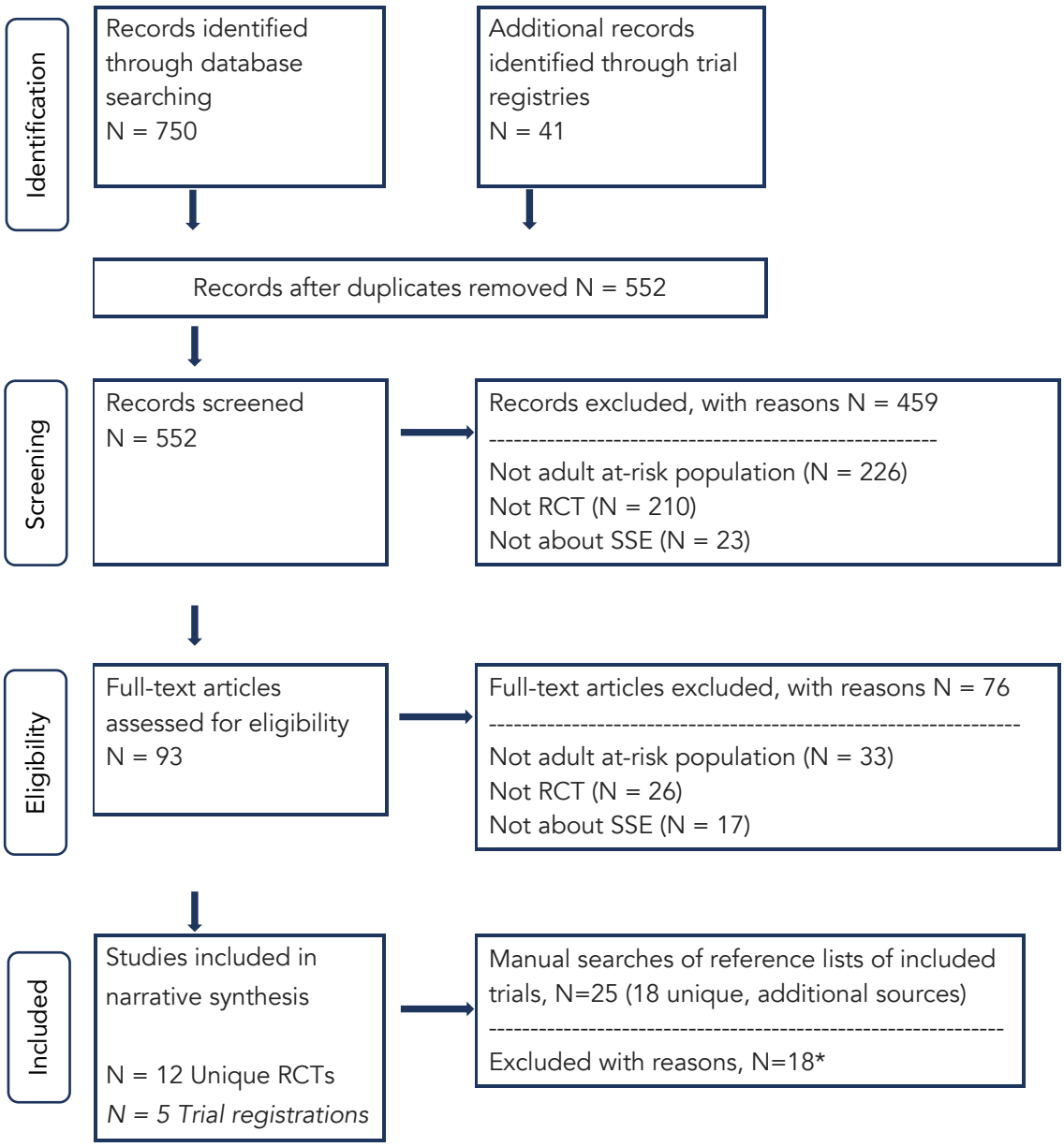

Figure 1. PRISMA flowchart of study selection.
Note. Adapted from Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., & and the Prisma Group. (2009). Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. Annals of Internal Medicine, 151(4), 264-269. doi:10.7326/0003-4819-151-4-200908180-00135
*Details of the manual searches and the reasons for exclusion are included in Appendix 4.

Appendix 1: Medline Search

Medline
Database(s): Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily, Ovid MEDLINE(R) and Ovid OLDMEDLINE(R) 1946 to Present
Search Strategy:

#	Searches	Results
1	Melanoma/ or melanoma.mp.	102432
2	self examination.mp. or Self-Examination/	3558
3	self exam*.mp.	3707
4	self screen*.mp.	151
5	self surveillance.mp.	57
6	self monitor*.mp.	8813
7	skin exam*.mp.	769
8	2 or 3 or 4 or 5 or 6 or 7	13364
9	skin neoplasms.mp. or Skin Neoplasms/	101285
10	skin cancer.mp.	13147
11	skin surveillance.mp.	41
12	8 or 11	13396
13	1 or 9 or 10	174715
14	12 and 13	766
15	randomized controlled trial.pt.	404274
16	controlled clinical trial.pt.	89994
17	randomi?ed.ab.	397618
18	placebo.ab.	165263
19	drug therapy.fs.	1810175
20	randomly.ab.	240295
21	trial.ab.	343550
22	groups.ab.	1504295
23	or/15-22	3643127
24	exp animals/ not humans.sh.	4173179
25	23 not 24	3133238
26	14 and 25	187

Appendix 2: Inclusion and Exclusion Criteria for Relevant Trials

Inclusion	Exclusion
(P) Population: • Individuals at increased risk for melanoma • Adults (18+) Increased Risk (environmental +bio factors): • Immunosuppressed individuals (radiation; transplant) • History of childhood radiation • Melanoma patients • People w/ a history of melanoma • Non-melanoma skin cancer (NMSC: BCC/SCC) patients • 100+ naevi (moles; birth or beauty marks) or 5+ atypical naevi • First degree relatives of melanoma patients • 50-100 naevi; • 1+ atypical naevi (http://www.dermnetnz.org/lesions/atypical-naevi.html) • Phenotypic features ▪ red or blond hair ▪ tendency to freckle ▪ gets easily burnt ▪ tanned skin	• General Population • Children/youth below 18 • Men 50+ • Spouses and other non-blood relatives of melanoma patients Other examples of non-eligible groups: • Beach-goers • University/college students • Patients presenting for routine medical visits • Healthcare professionals working in melanoma clinics • Parents of children treated for childhood cancers
(I) Intervention: • Design: Randomized controlled trial, with at least two groups • Content: Any Informational, educational, psychological, didactic intervention	• Design: Not an RCT Content: Medical procedures (pharmacological, surgery/biopsy)
(C) Comparison: • at least one other intervention or control arm	
(O) Outcomes: • SSE behaviour • Early detection • Mortality	• SSE not an outcome • SSE Accuracy as outcome (i.e., identifying problematic lesions accurately via SSE) • Any other outcomes
Language: • English, French, German, Spanish, Russian, Romanian	• Any other language

Note. NMSC = non-melanoma skin cancer; BCC= basal cell carcinoma; SCC= squamous cell melanoma

Appendix 3: Data Coding Sheet for Full Text Review

Refid: 1, There and Back Again: A Review of Residency and Return Migrations in Sharks, with Implications for Population Structure and Management.
Chapman DD, Feldheim KA, Papastamatiou Y, Hueter RE

The overexploitation of sharks has become a global environmental issue in need of a comprehensive and multifaceted management response. Tracking studies are beginning to elucidate how shark movements shape the internal dynamics and structure of populations, which determine the most appropriate scale of these management efforts.

Tracked sharks frequently either remain in a restricted geographic area for an extended period of time (residency) or return to a previously resided-in area after making long-distance movements (site fidelity). Genetic studies have shown that some individuals of certain species preferentially return to their exact birthplaces (natal philopatry) or birth regions (regional philopatry) for either parturition or mating, even though they make long-distance movements that would allow them to breed elsewhere. More than 80 peer-reviewed articles, constituting the majority of published shark tracking and population genetic studies, provide evidence of at least one of these behaviors in a combined 31 shark species from six of the eight extant orders.

Residency, site fidelity, and philopatry can alone or in combination structure many coastal shark populations on finer geographic scales than expected based on their potential for dispersal. This information should therefore be used to scale and inform assessment, management, and conservation activities intended to restore depleted shark populations. Expected final online publication date for the Annual Review of Marine Science Volume 7 is January 03, 2015.

1. **Population: Adults at Increased Risk for Melanoma?**
   - ◯ Yes
   - ◯ No

2. **Intervention type: RCT**

   Intervention content: psycho-educational, informational
   - ◯ Yes
   - ◯ No

3. **Outcome: SSE**
   - ◯ Yes
   - ◯ No

4. **Outcome: Early Detection?**

   (e.g., melanoma size, depth; melanoma stage)
   - ◯ Yes
   - ◯ No

5. **Outcome: Mortality or Survival?**
   - ◯ Yes
   - ◯ No

6. **Entry in Trial Registry?**
   - ◯ Yes
   - ◯ No

7. **Relevant Trial Registry Entry?**
   - ◯ Yes
   - ◯ No
   - ◯ N/A

Appendix 4: Results of Manual Searches of Reference Lists of Included Trial Reports

Summary of manual searches: N=25 articles referenced in the method sections/measures of the included trials:
- N=3 duplicate sources
- N=4 already included trial reports
- N=6 not about SSE
- N=12 correlates or predictors of SSE, but not study aim to establish validity of SSE measures

Included trial First author, year	Sources cited in method section of included trial report First author, year
Bowen, 2015 (Bowen et al., 2015)	1) Bowen et al. 2012# (Bowen et al., 2012) 2) Weinstock et al. 2007+ (Weinstock et al., 2007) 3) Weinstock et al. 2004*+ (Weinstock et al., 2004)
Geller, 2006, (Geller et al., 2006)	None provided
Glanz, 2010, (Glanz et al., 2010)	None provided
Glanz, 2013 (Glanz et al., 2013)	4) Glanz et al. 2003# (Glanz et al., 2003) 5) Glanz et al. 2010** (Glanz et al., 2010) 6) Nelson et al. 2004# (Nelson et al., 2004)
Glanz, 2015 (Glanz et al., 2015)	7) Glanz et al. 2010** (Glanz et al., 2010)
Glazebrook, 2006 (Glazebrook et al., 2006)	None provided
Manne, 2010 (S. Manne et al., 2010)	8) Manne et al., 2004+ (S. Manne et al., 2004) 9) Manne & Lessin, 2006+ (S. Manne & Lessin, 2006) 10) Oliveria et al., 1999+ (Oliveria et al., 1999) 11) Manne 2009# (S. L. Manne et al., 2009) 12) American Academy of Dermatology (AAD), 2006
Oliveria, 2004 (Oliveria et al., 2004)	13) Weinstock et al. 1999+ (Weinstock et al., 1999) 14) Weinstock et al. 2004*+ (Weinstock et al., 2004)
Rat, 2014, France (Rat et al., 2014)	15) Glanz et al. 2008+ (Glanz et al., 2008) 16) Global Solar UV Index: A Practical Guide: A joint recommendation of the World Health Organization, World Meteorological Organization, United Nations Environment Programme, and the International Commission on Non-Ionizing Radiation Protection# (www.who.int/uv/publications/en/UVIGuide.pdf)
Robinson, 2007 (Robinson et al., 2007a)	17) Robinson et al. 1998*+ (Robinson et al., 1998) 18) Robinson et al. 2002*+ (Robinson et al., 2002)

Robinson, 2010 (Robinson et al., 2010)	19) Robinson, 2007** (Robinson et al., 2007a) 20) Robinson et al. 2008[+] (Robinson, Stapleton, & Turrisi, 2008) 21) Robinson et al. 1998*[+] (Robinson et al., 1998) 22) Robinson et al. 2002*[+] (Robinson et al., 2002)
Turrisi, 2015 (Turrisi et al., 2015)	23) Boone et al. 2009[+] (Boone et al., 2009) 24) Robinson, Turrisi, Stapleton, et al., 2007[+] (Robinson, Turrisi, & Stapleton, 2007b) 25) Robinson, Turrisi, and Stapleton, 2007** (Robinson et al., 2007a)

Note. *Duplicate sources, cited in more than one trial report.
** Source coincides with one of the 12 trial reports included in this review.
[#] Not about SSE
[+] Predictors or correlates of SSE, but not aim to validate SSE measure/scale

Link Between Manuscripts 1 and 2

Manuscripts 1 and 2 share the same methodology, as they both report results from a systematic review of randomized controlled trials of behavioural interventions conducted with individuals at increased risk for melanoma. Manuscript 1 investigated how skin self-examination (or SSE) was operationalized, defined, and measured, in randomized controlled trials assessing behavioural interventions among individuals at an increased risk to develop melanoma. SSE was identified as one of the main outcomes in the trials included in the systematic review. This issue of SSE operationalization was important to address, since previous reports from the melanoma literature indicate that rates of SSE vary widely as a function of the modality of assessment for SSE behaviour. Manuscript 1 reports in detail the various modalities used to assess SSE across the trials included in our systematic review of interventions. We found inconsistent operationalizations of SSE and a lack of evidence supporting the validity and reliability of the items used to assess SSE across the included trials. These findings provided context for the interpretation of the results of manuscript 2, which evaluates the effect of interventions targeting SSE on several outcomes, including SSE behaviour.

Manuscript 2: The Effect of Behavioural Interventions for Individuals at Increased Risk for Melanoma: A Systematic Review of Randomized Controlled Trials

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Conflict of Interest

None of the authors declare any conflict of interest. Alan Geller was the senior author of the Geller, 2006 trial, which is one of the trials included in this review.

Authors' Contribution:

AC, BT, AK Designed the study.

AC, CM, CB Conducted study selection and data extraction.

AC conducted the data synthesis and completed the first draft of the manuscript.

CM, DR, BT, AG, AK Contributed critical feedback to earlier drafts for the manuscript, reviewed, and approved the final draft of the manuscript.

EK conducted the systematic search, reviewed, and approved the final draft of the manuscript.

All authors read and approved the final draft of the manuscript.

Abstract

Background

As tumour thickness is the best predictor of survival in melanoma, and most melanomas develop with a visible, pre-clinical phase, early detection has been proposed as a strategy to facilitate early treatment and reduce mortality. The aim of this systematic review was to assess the impact of behavioural interventions on mortality due to melanoma, melanoma early detection (defined as thin versus thick tumours), and preventive health behaviours, including skin self-examination (SSE), partner-assisted examination (PASE) and clinical skin examination (CSE).

Method

Data sources included MEDLINE, PsycINFO, EMBASE, CINAHL, Web of Science, the Cochrane Central Register of Controlled Trials, Proquest Dissertations and Theses and Conference Proceedings, and trial registries, searched from inception through February 17, 2017. Articles were included if they reported the results of RCTs of behavioural interventions with individuals at increased risk for melanoma, which had mortality, early detection, or preventive behaviours (e.g., SSE) as outcomes. Two independent reviewers carried out the study selection and conducted data extraction and quality assessment. Results were presented as a narrative synthesis.

Results

We identified 12 trials eligible for this review: none assessed mortality or early detection, but all assessed behavioural outcomes including SSE, PASE or CSE. There was some methodological heterogeneity between the trials, and risk of bias was unclear for many domains across the included trials. Problematic reporting made it difficult to differentiate between risk of bias inherent to trial design and reporting issues. The effects of studies assessing the behavioural outcomes as percentage of events endorsed were pooled as these trials were comparable in terms of intervention content and outcome assessment. Meta-analyses conducted separately for each of the three behavioural outcomes showed small significant effects on SSE when comparing active interventions against treatment as usual and no significant effects on PASE or CSE. The studies assessing

SSE, PASE and CSE via continuous outcomes could not be meta-analyzed due to large heterogeneity between trials.

Conclusions

As no randomized controlled trials assessing mortality or early detection were identified, it cannot be concluded whether behavioural interventions have an impact on these outcomes. Among the 12 RCTs, which assessed behavioural outcomes (SSE, PASE, CSE), we found some support for the efficacy of several behavioural interventions on SSE behaviour among at-risk individuals. Due to the heterogeneity present among the included trials, our results might not be generalizable beyond these trials. Several recommendations are made for improving both trial methodology and reporting, as per current standards.

Registration: PROSPERO (CRD42016033765).

Keywords: melanoma early detection, melanoma prevention, skin self-examination, behavioural interventions, RCT, systematic review

The Effect of Behavioural Interventions for Individuals at Increased Risk for Melanoma:

A Systematic Review of Randomized Controlled Trials

Skin cancers are the most frequently diagnosed cancers in the United States and Canada, and, among them, melanoma is the most lethal type (Erdei & Torres, 2010; Linos, Swetter, Cockburn, Colditz, & Clarke, 2009; Rogers, Weinstock, Feldman, & Coldiron, 2015). During 2011-2015, melanoma incidence was reported at 22.8 per 100,000 people per year; the mortality rate was 2.6 per 100,000 people; and estimates for 2018 include 91,270 new cases and 9,320 deaths from melanoma in the US (Howlader et al., 2016). Populations with an increased risk for melanoma include individuals with a personal history of the disease (Youlden, Youl, Soyer, Aitken, & Baade, 2014), first-degree relatives of melanoma patients (Gandini, Sera, Cattaruzza, Pasquini, Zanetti, et al., 2005), individuals with genetic mutations (CDKN2A gene) (Fargnoli, Gandini, Peris, Maisonneuve, & Raimondi, 2010), childhood survivors of cancer treated with radiation (Friedman et al., 2010), immuno-suppressed individuals, such as those undergoing transplant procedures (Hollenbeak et al., 2005), individuals with more than 100 nevi or with more than 5 atypical nevi (Gandini, Sera, Cattaruzza, Pasquini, Abeni, et al., 2005), and individuals with some phenotypic features, such as (blue) eye color or (red) hair color (Gandini, Sera, Cattaruzza, Pasquini, Zanetti, et al., 2005).

While mortality rates are slowly decreasing, potentially due to early detection and timely or better treatments, incidence rates have increased on average with 1.5% each year during the last 10-15 years. The 5-year survival rate is excellent (98.4%) for patients diagnosed with localized disease (stages 0-II), but only 22.5% for distant disease (stages III-IV) (Howlader et al., 2016). Tumour thickness or depth of invasion at diagnosis is the best predictor of survival (Baade et al., 2006; Balch et al., 2009; Eisemann et al., 2012; Green, Baade, Coory, Aitken, & Smithers, 2012). So, early detection and timely treatment (surgical excision of the tumour) are crucial to survival. Most melanomas develop with a visible, pre-clinical phase, which creates a window of opportunity for early detection via visual inspection by lay persons and health care professionals (Friedman, Rigel, & Kopf, 1985).

Screening for melanoma could, in principle, facilitate the detection of melanoma at a time when the prognosis is still excellent. Evidence-based screening, however, should be grounded in strong and reliable

evidence linking the screening programs to health outcomes (such as mortality/survival) and the accurate evaluation of benefits and costs or harms. Screening programs that are not evidence-based may lead to over-diagnosing and potentially unnecessary treatment of early stage tumours (Esserman, Thompson, & Reid, 2013; Welch & Black, 2010), and the burdening of patients and/or the healthcare systems (Grossman et al., 2018). Within the skin cancer prevention community, opinions about screening for melanoma are divided. There are claims that screening could lead to an inflation of early stage diagnosis and possibly to unnecessary treatment of possibly "indolent" tumours without having a positive impact on health outcome, such as mortality or survival. In fact, analyses with population surveillance data (US SEER database) found a positive association between increased biopsies and increased incidence rates of melanoma in situ (Weinstock et al., 2017; Welch, Woloshin, & Schwartz, 2005). The largest ecological (non-randomized) screening trial to date, the SCREEN study in Germany, found an increase in the incidence of early stage melanoma as a result of a 5-year population-wide screening campaign, a temporary reduction in mortality rates for the duration of the screening campaign (2003-2008), but a return to pre-screening mortality levels after the termination of the screening trial (Boniol, Autier, & Gandini, 2015; Katalinic et al., 2012; Katalinic, Eisemann, & Waldmann, 2015; Stang & Jöckel, 2016). To counter these findings, there are several arguments in support of screening for melanoma: a) data from the INFORMED program in the US, which trains physicians to effectively check the skin for melanoma, and found that well-trained physicians can be very accurate at diagnosing, which was reflected in stable biopsy rates compared to "standard of care" screening (Weinstock et al., 2016); b) harms due to screening have not been adequately assessed by previous research (Curiel-Lewandrowski & Swetter, 2016; Grossman et al., 2018); and c) the cost of treatment of advanced and terminal stage melanoma is drastically higher than the cost of treatment for earlier stages and most of the medical resources allocated to melanoma are being used up by patients diagnosed with advanced disease (Guy, Ekwueme, Tangka, & Richardson).

The current evidence supporting the efficacy of physician-led screening via visual inspection of the skin comes from a) large observational studies with the general population, which reported a reduction in mortality rates post screening (Aitken et al., 2002; Brunssen, Waldmann, Eisemann, & Katalinic, 2017; Katalinic et al., 2012; Schneider, Moore, & Mendelsohn, 2008); b) a large population-based case control study (78% of all

eligible melanoma cases diagnosed between 2000 and 2003 in Queensland, n=3762 and n=3824 controls) which found that a physician-led clinical skin exam (CSE) three years prior to diagnosis was associated with a 14% lower risk of a thick (advanced) tumour at diagnosis (Aitken, Elwood, Baade, Youl, & English, 2010); and c) smaller empirical, cross-sectional (survey) studies which also linked CSE to thinner tumours at diagnosis (De Giorgi et al., 2012; Pollitt et al., 2009; Swetter, Pollitt, Johnson, Brooks, & Geller, 2012). Furthermore, empirical cross-sectional studies have found that patients and family members detected up to 50-80% of all melanomas (Carli et al., 2003; De Giorgi et al., 2012; Swetter et al., 2012), increased thoroughness (or extent of skin covered during) of the skin self-exam was associated with thinner lesions (Pollitt et al., 2009), and patients who examined at least some parts of their body had thinner lesions at diagnosis compared to those who did not examine their skin (Carli et al., 2003; Pollitt et al., 2009). A case control study (423 melanoma patients and 678 matched controls) found that individuals who conducted SSE were twice as likely to self-detect melanoma and less likely to have thick (advanced) tumours at diagnosis compared to those who did not practice SSE (Titus et al., 2013).

Clinical practice guidelines for melanoma prevention and melanoma follow-up and care promoted by various organizations recommend that individuals at increased risk for melanoma should be provided written or verbal information about self-examination and physicians should periodically examine the skin of high-risk individuals (Marciano, Merlin, Bessen, & Street, 2014; Watts et al., 2015). Consistent with clinical guidelines for the prevention and management of melanoma, expert clinicians and findings from empirical studies support a complementary approach to the secondary prevention of melanoma detection, which involves self-surveillance of the skin (or skin self-examinations [SSE]) and physician-led skin examinations for individuals at increased risk (or clinical skin exams [CSE]) (Curiel-Lewandrowski, Chen, & Swetter, 2012; De Giorgi et al., 2012; Friedman et al., 1985; Geller, Swetter, Oliveria, Dusza, & Halpern, 2011; Robinson & Halpern, 2016; Robinson & Jablonski, 2018; Svoboda, Friedman, & Rigel, 2018; Swetter et al., 2012).

Research Objectives and Rationale

The overall goal of the current review is to provide a comprehensive overview of the available evidence for intervention strategies that promote SSE and CSE, and to determine if interventions that are effective at

facilitating these behaviours are also resulting in early detection and decreased melanoma-related mortality.

Our study focuses on non-pharmacological, behavioural interventions developed for individuals at an increased risk to develop melanoma compared to the general population. Two other systematic reviews of melanoma prevention interventions were published in the last two years. Wu and colleagues (Wu et al., 2016) reviewed a total of 20 studies assessing the efficacy of interventions on melanoma preventive behaviours (sun protection, skin self-examination and physician-led skin examination) among adult and pediatric populations with a personal or family history of melanoma. The review included randomized controlled trials and other study designs. Among the 12 studies included in this review and which assessed the effect of interventions on SSE behaviour, 9 found significant positive effects for the active arm, which suggests that some interventions are efficacious at increasing SSE behaviour. A second systematic review conducted by Henrikson and colleagues (Henrikson et al., 2018) assessed the effect of "primary-care relevant" interventions among various populations with high risk for melanoma and the general population (with the exception of individuals with a personal history of melanoma). This review, which included randomized and non-randomized clinical trials, identified no trials assessing the effect of interventions on melanoma-related mortality or melanoma early detection. However, the review identified 11 trials assessing the impact of psycho-social interventions on SSE behaviour among adults, of which 9 reported significant treatment effects.

The objective of the current study is to evaluate the effect of behavioural interventions on three distinct outcomes, melanoma mortality, melanoma early detection, and melanoma preventive behaviours among at risk individuals. The scope of the current review overlaps with that of the previous two reviews. However, the methodology of our review, which was pre-registered, is somewhat different: we included all of the populations with an increased risk of melanoma compared to the general population (but excluded studies with the general population) and focused solely on randomized controlled trials. Specifically, the current study is a systematic review of randomized controlled trials of behavioural interventions for individuals at increased risk for melanoma, including those with a personal or familial history of the disease. We focused on trials that tested interventions that included an educational component about SSE behaviour.

Primary Research Questions

1) Compared to an inactive control group (e.g., usual care, attention control), do behavioural interventions for individuals at increased risk for melanoma decrease melanoma-related mortality?
2) Are some behavioural interventions for individuals at increased risk for melanoma more effective than others at decreasing melanoma-related mortality?

Secondary Research Questions

1) Compared to an inactive control group (e.g., usual care, attention control), do behavioural interventions for individuals at increased risk for melanoma increase a) melanoma early detection, b) skin self-examination, and c) clinical skin examination?
2) Are some behavioural interventions for individuals at increased risk for melanoma more effective than others at increasing a) melanoma early detection, b) skin self-examination, and c) clinical skin examination?

Method

This systematic review was registered with the International Prospective Register of Systematic Reviews (Prospero ID: CRD42016033765). The review was conducted in line with the AMSTAR checklist (Shea et al., 2007) and adhered to the PRISMA reporting guideline (Moher, Liberati, Tetzlaff, Altman, & and the Prisma Group, 2009).

Search Strategy

The search strategy was developed by a research librarian (EK) in collaboration with the research team and was peer-reviewed by a second librarian. Medline, EMBASE, CINAHL, PsycINFO, Web of Science, and the Cochrane Central Register of Controlled Trials were searched from inception to February 2017. The following trial registries were also searched: Clinicaltrials.gov, UK Clinical Trails Gateway, International Clinical trials Registry Platform Search Portal, and the Australian and New Zealand Clinical Trials Registry. The search strategy (see Appendix 1) was developed for Medline and adapted to the remaining databases. Results from all databases were imported into EndNote, where duplicate removal was performed. Next, results were imported into DistillerSR where study selection was performed.

Identification of Eligible Studies

Population. Adults (18 years of age or older) at increased risk for melanoma as defined by primary studies (e.g., patients with a personal history of melanoma; first degree relatives of melanoma patients; immunosuppressed individuals; survivors of childhood cancers treated with radiation; individuals with phenotypic features such as freckles, fair skin or hair color, presence of more than 5 nevi). We decided to include studies with individuals with a past melanoma diagnosis, who are at risk to develop subsequent new primary (unrelated to their previous diagnosis) melanomas alongside studies with individuals at increased risk to develop the disease because the prevention needs of these groups are arguably similar. Studies were excluded if the study population was not at greater risk for developing melanoma than the general population. If a study included a mixed population of eligible and non-eligible individuals (e.g., melanoma patients and their partners or individuals below and over 18 years of age), we included the study if the eligible individuals could be differentiated from the non-eligible individuals and if results were provided separately for our population of interest. For a detailed list of risk categories and eligibility criteria, please refer to Appendix 2.

The current review focused on populations with an increased risk of melanoma incidence, primarily because the recommendations for the prevention of melanoma, as currently defined by North American clinical practice guidelines, are similar across these groups. We therefore excluded studies with a general population, such as studies conducted with primarily Caucasian populations, who are arguably at higher risk for melanoma than populations of colour, and with Caucasian men > 50 years of age, who are at higher risk of dying from melanoma than any other group. Notably, most intervention studies conducted with the general population and men > 50 years of age were conducted in Australia, which has the highest incidence of melanoma in the world. This review aims to inform public health policy in Canada and the United States, where melanoma incidence is much lower than in Australia and the clinical guidelines consistently recommend SSE only for population at higher risk compared to that of the general population.

Interventions. Eligible interventions included informational, behavioural, psychological, or non-pharmacological, medical procedures delivered by medical professionals or trained research assistants

targeting the early detection (or secondary prevention) of melanoma. In order to differentiate between the many content categories (or strategies) used in the trials, we used the following criteria:

a) Informational strategies (Info) included the passive (e.g., pamphlet) and interactive (in person) delivery of information regarding melanoma (e.g., prevalence, incidence, recurrence rates, risk factors for melanoma) or regarding the importance of primary and secondary prevention (skin self-exams, clinical exams). The simple delivery of melanoma prevention information, verbally or in a pamphlet, is the least resource-intensive intervention used in melanoma prevention studies and also represents "the standard of care" in most clinical settings.

b) Behavioural strategies (Skills) included demonstrating what skin exams involve, such as checking the skin with the help of a partner, using mirrors or magnifying glasses, or showing how to apply the ABCDE criteria to identify problematic lesions by evaluating the Asymmetry, Border, Color, Diameter, and Evolution of lesions; having participants work through exercises to identify problematic lesions either on their skin or using melanoma pictures; and discussions about how/when to ask for a clinical exam. Teaching preventative behavioural skills is different from providing prevention information alone in that they involve active versus passive engagement of participants, which might differentially impact health behaviour change (Fisher & Fisher, 1992; Fisher & Fisher, 1993).

c) Psychological strategies (Psych) refer to the use of psychotherapeutic techniques, such as guided imagery, motivational interviewing, or stress-reduction strategies to target specific barriers to performing SSE or asking for skin exams. Previous literature has shown that common barriers to health behaviour change include limited motivation to perform the new behaviour, low readiness to change, negative attitudes towards and low intentions to adopt the new behaviour (Prochaska & Velicer, 1997). In healthcare settings, these characteristics are often targeted using specific intervention techniques such as motivational interviewing (Rollnick, Miller, Butler, & Aloia, 2008) or stress-reduction strategies (e.g., mindfulness-based therapy) (Piet, Würtzen, & Zachariae, 2012).

d) Medical strategies (Med) refer to the delivery of preventive and early detection procedures by a medical professional, including clinical skin exams (typically done by a general practitioner or dermatologist), giving feedback on genetic test results, or counselling on genetic risk.

Comparison: Primary and secondary research question #1: any non-active control (e.g., standard of care, treatment as usual [TAU]; attention control; no treatment). Primary and secondary research question #2: any other active comparator. We used the same intervention components described above to categorize the types of control arms used in the trials.

Outcomes. (1) Mortality due to melanoma.

(2) Earlier detection of melanoma will be conceptualized as a significant difference in the mean thickness of melanoma when comparing the active intervention arm to the control arm; or increased diagnoses of stage 0-II melanomas and decreased diagnoses of stages III-IV when comparing the active intervention arm to the control arm.

(3) SSE behaviour will be assessed in terms of frequency (i.e., how often was SSE performed?) and comprehensiveness (i.e., were all body parts examined, including hard to reach areas, such as head, genital areas and the back? was a mirror used for hard to reach areas? was someone else helping with the exam?).

Post hoc, during the data extraction phase, we decided to extract data and report on two additional outcomes, partner-assisted SSE (PASE) and physician-led clinical skin exam (CSE). Once the decision to include these additional outcomes was made, all of the relevant trials were re-evaluated specifically for content relevant to these additional outcomes. PASE refers to the practice of skin self-examination conducted with the help of a partner and is arguably similar to SSE, but since some trials reported these two outcomes separately, we decided to treat them separately as well. We added the CSE outcome to our review given arguments from the melanoma scholarly literature that a combination of SSE and CSE would provide a more realistic or more beneficial approach to the secondary prevention of melanoma than SSE alone (Curiel-Lewandrowski et al., 2012; Robinson & Halpern, 2016; Swetter et al., 2012).

Study Design. RCTs. Studies with any other study design were excluded.

Study Selection

Two raters (AC, CM) independently reviewed the titles and abstracts of all identified citations using predetermined coding sheets created in a specialized software for systematic reviews, Distiller SR (Evidence Partners, 2017). If either one of the raters deemed an abstract as potentially eligible, a full-text review was undertaken independently by the same two raters. Disagreements after the full text review were resolved by consensus between the raters, with consultation with a third team member (AK or BT) as necessary. Distiller-formatted data screening sheets for titles and abstracts and full text review, respectively, were included in Appendix 3.

Data Extraction Process

Three raters (AC, CM, CB) independently extracted data from relevant trials using pre-designed forms in Excel. Data extracted included study characteristics (authors, year of publication, country of study, funding source, trial registration number), patient characteristics (population and eligibility criteria, number per group), patient demographics (age in years, gender), interventions and comparators (description of intervention components, duration, administration method, and expertise/training required to administer the intervention, setting), and outcomes (definition/operationalization, timeframe of assessment, and timing of follow-up assessment). We also extracted trial specific data such as trial design and hypotheses, planned outcome analyses (as per trial registration if available, and/or per method section/data analysis plan), attrition rates, intention-to-treat procedures (pre-specified and actually conducted), handling of missing data (pre-specified and conducted) to inform the risk of bias assessment (see below) and measures of effect available at all time points to inform our analyses and to answer our research questions. For continuous outcomes, we collected N, means, and standard deviations for each arm. For dichotomous outcomes, we collected N, number of events, and percentage for each arm. Disagreements were resolved by consensus with a fourth investigator (AK) consulted if necessary.

Risk of Bias Assessment

Using Cochrane's Risk of Bias Tool, two reviewers (AC, CM) independently appraised the risk of bias of the included studies, as it pertains to the outcomes of interest. This instrument includes seven questions, each

pertaining to a different methodological domain (i.e., Random Sequence Generation, Allocation Concealment, Blinding of Participants and Personnel, Blinding of Outcome Assessment, Incomplete Outcome Data, Selective Reporting of Outcomes, and Other Areas of Bias). For each domain and for each outcome, reviewers rated "high-risk", "low risk" or "unclear risk" and recorded the answers using a pre-designed excel form. The justification of the rating for each domain was entered in free-form comments and was supplemented with a citation from the trial report, when necessary. Disagreements were resolved by consensus, with a third investigator consulted (AK), if necessary.

Assessment of Heterogeneity

Clinical heterogeneity was investigated by comparing the included trials with respect to differences in population risk factors, eligibility criteria and patient demographics. Methodological heterogeneity was investigated by exploring a) intervention content, frequency and duration, and b) outcome definition and timeframe of assessment (e.g., "behaviour performed during last 6 months"). When evaluating differences between trials, we differentiated between two comparisons (active intervention versus non-active control and active intervention versus active control), as per our research questions. If clinical and methodological heterogeneity were found to be low, statistical heterogeneity was to be investigated by assessing the magnitude of the intervention effects (confidence intervals) and by computing chi square and I square statistics in RevMan 5.3.4 (The Cochrane Collaboration, 2014). The Cochrane Handbook for Systematic Reviews of Interventions recommends the following guidelines when interpreting the I square statistic: 0-40% "might not be important", 30-60% "might be moderate heterogeneity", 50-90% "may be substantial heterogeneity", 75-100% "considerable heterogeneity".

Data Presentation and Synthesis

All study characteristics were summarized in tabular form to facilitate inspection and discussion in terms of study heterogeneity, grouping of interventions, and other topics required to inform analysis. Provided there was limited clinical and methodological heterogeneity between studies, meta-analytical methods were to be used to derive a statistical summary (standardized mean differences and odds ratios, with 95% confidence intervals) representing the combined result of all studies evaluating the effect of interventions on the key

outcomes. If meta-analyses were not appropriate, a narrative synthesis was planned with detailed findings reported in tabular format. To assist with the interpretation of findings forest plots were created using RevMan 5.3.4.

Results

Results of the Search

The electronic database search identified 552 unique citations, of which 459 were excluded after reviewing titles and abstracts and 76 after the full-text review. At both stages, we excluded articles based on the following criteria: a) if the population was not at risk, b) if the study design was not RCT, and c) if the study did not assess any of the outcomes of interest: mortality, early detection, or behavioural outcomes (SSE, PASE. CSE). If it was unclear whether a study met the exclusion criteria based on the title and abstract, it was included in the full-text review and re-assessed using the above-mentioned criteria. The full-text review was performed for 93 article and we identified a total of 12 unique RCTs as eligible for inclusion in this systematic review study (see Fig 1 for PRISMA Flow Diagram).

Characteristics of the Included Trials

Table 1 summarizes the characteristics of the included trials. Of the 12 trials, 10 were conducted in the United States (Bowen, Burke, Hay, Meischke, & Harris, 2015; Geller et al., 2006; Glanz, Schoenfeld, & Steffen, 2010; Glanz et al., 2015; Glanz et al., 2013; Manne et al., 2010; Oliveria et al., 2004; Robinson, Turrisi, Mallett, Stapleton, & Pion, 2010; Robinson, Turrisi, & Stapleton, 2007; Turrisi, Hultgren, Mallett, Martini, & Robinson, 2015), 1 in the United Kingdom (Glazebrook, Garrud, Avery, Coupland, & Williams, 2006), and 1 in France (Rat et al., 2014); 11 reported funding from national/federal funding agencies (Bowen et al., 2015; Geller et al., 2006; Glanz et al., 2010; Glanz et al., 2015; Glanz et al., 2013; Glazebrook et al., 2006; Manne et al., 2010; Rat et al., 2014; Robinson et al., 2010; Robinson et al., 2007; Turrisi et al., 2015) and 1 did not report any funding (Oliveria et al., 2004). Four trials were published before 2010 and 8 trials were published between 2010-2015. The populations included in the trials were melanoma patients (n=4) (Bowen et al., 2015; Robinson et al., 2010; Robinson et al., 2007; Turrisi et al., 2015), first degree relatives of melanoma patients (n=2) (Geller et al., 2006; Manne et al., 2010), and at-risk individuals recruited in primary care outpatient clinics (n=6) (Glanz et al., 2010;

Glanz et al., 2015; Glanz et al., 2013; Glazebrook et al., 2006; Oliveria et al., 2004; Rat et al., 2014). Eligibility criteria for the at-risk outpatients included phenotypic features associated with increased risk for melanoma, number of atypical moles, and personal and/or familial history of melanoma (see Table 1). The minimum number of patients randomized per condition was 19 (Robinson et al., 2010) and the maximum was 362 (Glanz et al., 2010). Six trials were individually randomized controlled trials (Glanz et al., 2010; Glanz et al., 2015; Oliveria et al., 2004; Robinson et al., 2010; Robinson et al., 2007; Turrisi et al., 2015) and 6 were cluster RCTs (Bowen et al., 2015; Geller et al., 2006; Glanz et al., 2013; Glazebrook et al., 2006; Manne et al., 2010; Rat et al., 2014). Eight trials compared an active intervention to a non-active control (Bowen et al., 2015; Geller et al., 2006; Glanz et al., 2010; Glanz et al., 2015; Glanz et al., 2013; Glazebrook et al., 2006; Rat et al., 2014; Turrisi et al., 2015) and 5 trials compared an active intervention to an active control (Manne et al., 2010; Oliveria et al., 2004; Robinson et al., 2010; Robinson et al., 2007; Turrisi et al., 2015). Turrisi and colleagues (Turrisi et al., 2015) reported both types of comparisons, so this trial was included in our review of both comparisons.

Primary Research Questions: Mortality Outcome. No studies met the inclusion criteria.

Secondary Research Questions: Early Detection of Melanoma, SSE, PASE, CSE. No studies met the inclusion criteria for the early detection of melanoma outcome. Seven trials met the inclusion criteria for the SSE outcome (Bowen et al., 2015; Geller et al., 2006; Glanz et al., 2010; Glanz et al., 2015; Glanz et al., 2013; Glazebrook et al., 2006; Rat et al., 2014), 5 met the criteria for the PASE outcome (Geller et al., 2006; Glazebrook et al., 2006; Robinson et al., 2010; Robinson et al., 2007; Turrisi et al., 2015), and 5 for the CSE outcome (Bowen et al., 2015; Geller et al., 2006; Glanz et al., 2015; Glanz et al., 2013; Manne et al., 2010).

Risk of Bias Assessment

Tables 2 and 3 provide the results for the risk of bias assessment for the individual and cluster RCTs, respectively. The risk of bias assessment per outcome led to ratings of low or unclear risk. An "unclear' rating was assigned in cases where there was lack of clarity or insufficient detail in the reporting of trial procedures. Further, only 5 trials (Glanz et al., 2015; Manne et al., 2010; Rat et al., 2014; Robinson et al., 2007; Turrisi et al., 2015) had been registered, of which one trial was registered before commencement of participant recruitment (Glanz et al., 2015), three trials were registered after recruitment began (Manne et al., 2010; Rat et al., 2014;

Turrisi et al., 2015), and one trial published results before it was registered on ClinicalTrials.gov (Robinson et al., 2007). None of the registered trials had pre-specified data analyses plans for the outcomes of interest and two trials (Rat et al., 2014; Turrisi et al., 2015) did not register any of our outcomes of interest (SSE, PASE, or CSE). We also identified problems consistent across all trials which are inherent to this field of research, as it pertains to the assessment of the behavioural outcomes: a) the use of self-report measures makes the blinding of the outcome assessment difficult, if not impossible; b) the use of unvalidated measures to assess the outcomes.

Assessment of Heterogeneity: Feasibility of Meta-Analyses

Active intervention versus non-active control. Table 4 provides the results of the assessment of heterogeneity for the trials comparing an active intervention to a non-active control. The intervention content was comparable across the relevant trials, with some variations present. The active components included prevention-focused interventions, which were delivered via pamphlets in all of the 8 relevant trials (Bowen et al., 2015; Geller et al., 2006; Glanz et al., 2010; Glanz et al., 2015; Glanz et al., 2013; Glazebrook et al., 2006; Rat et al., 2014; Turrisi et al., 2015), with the addition of a) psychological counselling on barriers to screening in one trial (Geller et al., 2006), b) genetic counselling in one trial (Glanz et al., 2013), c) clinical skin exams delivered by primary physicians in one trial (Rat et al., 2014), and d) demonstration of how to apply the ABCDE criteria to self-screening and periodic clinical skin exams delivered by dermatologists in one trial (Turrisi et al., 2015). The overall intervention duration (15-60 min) and intensity (1-4 sessions) were comparable across trials. The behavioural outcomes were scored as binary (proportion of events endorsed) or continuous (means and standard deviations) variables. Results were comparable across trials reporting binary outcomes (e.g., at least one SSE during a specified time period) (Bowen et al., 2015; Geller et al., 2006; Glanz et al., 2010; Glazebrook et al., 2006; Rat et al., 2014), but not across the trials reporting continuous variables, given the different ranges used to score the outcomes (0 to 4 times or more often; "never" to "last month") (Glanz et al., 2015; Glanz et al., 2013; Turrisi et al., 2015). There were some variations with respect to the timing of the follow-up assessment, but all trials used one assessment point at 3-6 months follow-up.

For the 5 trials reporting binary outcomes (Bowen et al., 2015; Geller et al., 2006; Glanz et al., 2010; Glazebrook et al., 2006; Rat et al., 2014), we completed a random-effects meta-analysis with Mantel-Haenszel

statistical method using odds ratios (OR) and 95% confidence intervals as measures of effect. We used data from the time point that was closest to the 4-month mark to allow for better comparisons between trials. Four of these trials were cluster RCT's (Bowen et al., 2015; Geller et al., 2006; Glazebrook et al., 2006; Rat et al., 2014) and one was an individual RCT (Glanz et al., 2010). In order to combine the effects from these types of trials, we adjusted the sample sizes and the proportion of endorsed events by the design effect, as per Cochrane collaboration recommendations (S. Green & Higgins, 2011). The design effect is calculated using a formula that incorporates the average cluster size and the intra-cluster correlation (ICC). As none of the cluster trials reported the ICC coefficient, but one trial used an ICC estimate of 0.02 for power and sample size calculations (Geller et al., 2006), we used the same estimate to compute adjustments for all cluster RCTs. Our decision is consistent with empirical findings, which suggest that estimates for ICC for trials assessing patient outcomes in primary care are lower than 0.05 (Campbell, Grimshaw, & Steen, 2000).

Given the heterogeneity with respect to the outcome assessment among the trials reporting continuous outcomes, results could not be synthesized meta-analytically. Instead, a narrative synthesis is provided, which is complemented by forest plots (without pooling of effects) using standardized mean differences (SMD) (Cohen's d) and 95% confidence intervals.

Active intervention versus active control. Table 5 reports the assessment of heterogeneity for the trials comparing an active intervention to an active control. In the 5 relevant trials (Manne et al., 2010; Oliveria et al., 2004; Robinson et al., 2010; Robinson et al., 2007; Turrisi et al., 2015), the intervention components in the active intervention arm and the active control arm included prevention-focused components delivered via pamphlets and demonstration of how to apply the ABCDE criteria to self-screening for melanoma, with the addition of a) counselling sessions in two trials (Manne et al., 2010; Oliveria et al., 2004) and b) periodic clinical skin exams delivered by dermatologists in one trial (Turrisi et al., 2015). However, one trial tested an intervention including prevention information, self-screening skills, and a counselling session against a comparator that included only prevention information and self-screening skills (Manne et al., 2010). Another trial tested tested an intervention with information, self-screening skills using a photobook, and a counselling session against a comparator with information, self-screening skills using a body map, and a counselling session

(Oliveria et al., 2004). Three trials compared identical intervention content between the active and control conditions, but delivered in different formats: to patient and partner versus patient alone (Robinson et al., 2010; Robinson et al., 2007) or delivered via workbook or Tablet versus delivered in person (Turrisi et al., 2015). Intervention duration and intensity and outcome assessment were comparable across trials. However, the components used across these 5 trials and the modality of delivery of the interventions were too different for the trials to be comparable using meta-analytic procedures. A narrative synthesis is provided instead, which is complemented by forest plots (without pooling of effects) computed with data from the 3- or 4-month follow-up. We used odds ratios (OR) and 95% confidence intervals as measures of effect for dichotomous outcomes and standardized mean differences (SMD) (Cohen's d) and 95% confidence intervals for continuous outcomes.

Intervention Effects on Behavioural Outcomes: SSE, PASE and CSE

Secondary research question 1: Comparison of active intervention versus non-active control. As illustrated in Figure 2, meta-analysis revealed a significant main effect of interventions on SSE behaviour: participants in the active conditions (n=817) were approximately 2 times more like than controls (n=828) to have performed SSE following the intervention (OR = 1.75, 95% CI [1.40, 2.20], z = 4.89, $p < .001$. The statistical heterogeneity among the included studies (n=5) was low, $I^2 = 8\%$, $chi^2(4) = 4.34$, $p = .36$. Meta-analysis revealed a non-significant effect of interventions on PASE (OR=1.21, 95% CI [0.81, 1.81]) and CSE (OR=1.09, 95% CI [0.76, 1.58]). A funnel plot included in Figure 3 illustrates the possibility of publication bias.

Figures 2 and 4 include the forest plots summarizing the intervention effects for relevant trials that reported dichotomous and continuous outcomes, respectively. Of the 7 studies comparing active interventions to treatment as usual (TAU) on SSE, 4 trials showed significant intervention effects (Bowen et al., 2015; Glanz et al., 2015; Glanz et al., 2013; Rat et al., 2014) and 3 did not show significant effects (Geller et al., 2006; Glanz et al., 2015; Glazebrook et al., 2006). Bowen and colleagues (Bowen et al., 2015) tested a prevention-focused informative intervention delivered via a website against a waitlist control among melanoma patients (n=157 active, n=156 control) and found that the active participants were almost 3 times more likely to have performed an SSE in the previous 2 months compared to controls (OR=2.88, 95% CI 1.67, 4.98). Glanz (Glanz et al., 2010) tested an information-based prevention intervention tailored to participants' personal risk factors and

preventive behaviours against TAU among at-risk outpatients (n=307 active, n=289 control). This trial found that participants in the active group were 1.6 times more likely to have performed an SSE in the last 3 months compared to controls (OR=1.55, (5% CI 1.00, 2.18). Rat and colleagues (Rat et al., 2014) compared an information-based prevention intervention, which also included a clinical skin exam (CSE) delivered by a physician, against TAU among at-risk outpatients in primary care (n=84 active, n=66 control; sample size adjusted for cluster design). This trial found that patients in the active group were almost twice as likely to have performed an SSE in the last 12 months (OR=1.93, 95% CI 1.00, 2.20). Of note, the timeframe for follow-up for this trial was only 5 months, which conflicts with the reported timeframe of assessment for SSE, which was 12 months. Glanz and colleagues (Glanz et al., 2013) compared an intervention including prevention-focused information tailored to personal risk factors, provision of genetic test results, and genetic counselling against TAU among at-risk outpatients enrolled in a cohort of families with a melanoma-history, who had undergone genetic testing for gene CDKN2A (n=34 active, n=37 control; sample size adjusted for cluster design). This trial found significant standardized mean differences (SMD) between active participants and controls in favour of the active intervention (SMD=0.65, 95% CI 0.17, 1.13). Of note, more than half of the participants randomized to the active intervention group did not attend the intervention. The trials with non-significant treatment effects on SSE tested a multi-component intervention involving information about general and personal risk factors for melanoma, skills about preventive behaviours, and barriers to self and physician-led skin exams against TAU among siblings of melanoma patients (n=149 active, n=165 control) (Geller et al., 2006); an information-based prevention intervention tailored to personal risk among at risk outpatients (n=113 active, n=97 control, sample size adjusted for cluster design) (Glazebrook et al., 2006); and an information-based intervention tailored to personal risk against TAU among at-risk outpatients (n=83 active, n=109 control) (Glanz et al., 2015).

Of the 2 studies comparing active interventions to non-active controls on PASE, one trial found significant treatment effects (Turrisi et al., 2015) and one did not (Geller et al., 2006). Turrisi and colleagues (Turrisi et al., 2015) evaluated the effect of an intervention delivered in three different formats, in person (n=139), via a workbook (n=134), and via an electronic tablet (n=59), against TAU (n=88) among melanoma patients. The interventions included identical content: generic prevention information, skills training on how to

perform a skin exam, and periodic clinical skin exams. The trial found significant differences between each of the three active conditions and the control, in favour of the active conditions: in person (SMD=1.48, 95% CI 1.18, 1.78), workbook (SMD=1.43, 95% CI 1.13, 1.73), and tablet (SMD=1.32, 95% CI 0.95, 1.68). None of the 4 trials assessing CSE found a significant intervention effect on this outcome (Bowen et al., 2015; Geller et al., 2006; Glanz et al., 2015; Glanz et al., 2013).

Secondary research question 2: Active intervention versus active control. Figures 5 and 6 include the forest plots summarizing the intervention effects for relevant trials that reported dichotomous and continuous outcomes, respectively. Of the 3 studies comparing active interventions to active controls on SSE, 2 trials showed significant intervention effects (Oliveria et al., 2004; Robinson et al., 2007) and one trial did not show significant effects (Manne et al., 2010). Oliveria and colleagues (Oliveria et al., 2004) tested an intervention with information, self-screening skills using a photobook, and a counselling session against a comparator with information, self-screening skills using a body map, and a counselling session among at-risk outpatients (n=49 active, n=51 control). This trial found that participants in the active intervention group were almost 3 times more likely than controls to have performed at least 3 SSE's in the last 4 months (OR=2.66, 95% CI 1.19, 5.96). Robinson and colleagues (Robinson et al., 2007) tested two identical interventions among melanoma patients (n=65 active, n=65 control), delivered to patients and their spouses (dyadic) versus patients alone (solo). This trial found significant standardized mean differences (SMD) between active intervention arm participants and controls in favour of the dyadic intervention (SMD=0.94, 95% CI 0.58, 1.30). The trial with non-significant treatment effects on SSE compared an intervention with a prevention pamphlet, self-screening skills, and a counselling session on personal risk and barriers to screening against a comparator including just the pamphlet and the self-screening skills (Manne et al., 2010).

Of the 3 studies assessing the impact of active interventions versus active controls on the PASE outcome, two studies showed significant treatment effects (Robinson et al., 2010; Robinson et al., 2007) and one study with two comparisons (workbook versus in person and tablet versus in-person) did not show significant results (Turrisi et al., 2015). Robinson and colleagues (Robinson et al., 2007) tested two modalities of delivering the same intervention content (pamphlet and self-screening skills) to patients and partners (dyad)

versus to patients alone and found significant mean differences between the groups in favour of the dyadic group (SMD=0.98 , 95% CI 0.61, 1.34) . A second study by Robinson and colleagues (Robinson et al., 2010) also tested two modalities of delivering the same intervention content (prevention information and self-screening skills) via workbook or in person and found significant mean differences between the groups in favour of the active intervention group (workbook) (SMD=2.25, 95% CI 1.44, 3.06). Turrisi and colleagues (Turrisi et al., 2015) also compared interventions with similar content (information, self-screening skills and clinical exams by dermatologist) delivered in different formats (workbook, tablet, and in person) and found no difference between the active intervention conditions (workbook, tablet) and the active control (in person). Importantly, the studies showing significant effects were severely underpowered, with 19/20 (Robinson et al., 2010) and 65/65 (Robinson et al., 2007) participants randomized to active and control arms, as was one arm (Tablet) in the Turrisi trial (Turrisi et al., 2015).

The one study assessing intervention effects on CSE reported a significant intervention effect on this outcome (Manne et al., 2010). As described previously, this trial compared an intervention with a prevention pamphlet, self-screening skills, and a counselling session on personal risk and barriers to screening against a comparator including just the pamphlet and the self-screening skills.

Discussion

This systematic review aimed to evaluate the impact of behavioural interventions compared to controls among people at increased risk for melanoma on the following outcomes: mortality due to melanoma, melanoma early detection, and several melanoma preventive behaviours, i.e., skin self-examination, partner-assisted skin examination, and physician-led (or clinical) skin examination. Our review did not identify any randomized controlled trials assessing mortality (primary research questions) or early detection (secondary research question) among populations with an increased risk to develop melanoma. Randomized controlled trials of interventions provide Level II evidence, second only to systematic reviews and meta-analyses of randomized controlled trials (McNair & Lewis, 2012). An RCT designed to assess melanoma-related mortality and early detection of melanoma faces several obstacles: 1) it would require a large sample size, which could only be achieved through multi-center, multi-country collaborations, which are very resource and time-

intensive. However, guidelines of care for melanoma differ between countries, rendering such research highly unfeasible; 2) it would require a 5 to 10-year follow-up. For example, among melanoma survivors, who have a 9-fold increased risk to develop a subsequent primary melanoma compared to the general population, 5.9% of melanoma recurrences are diagnosed within 5-10 years of the first melanoma (Bradford, Freedman, Goldstein, & Tucker, 2010) and 6.8 % and 11.3% of recurrences occur 15 and 25 years, respectively, after an initial diagnosis (Faries, Steen, Ye, Sim, & Morton, 2013). Given these considerations, it seems unlikely that an adequately powered RCT with an appropriate design and sufficiently long follow-up will be conducted in the near future (Robinson & Jablonski, 2018; Svoboda et al., 2018). As such, the next best levels of evidence could only come from non-randomized clinical trials (which face similar obstacles to those of the randomized clinical trials) and from large observational studies, cohort studies, and case-control studies (McNair & Lewis, 2012).

This review identified 12 trials assessing behavioural outcomes previously hypothesized to contribute to the early detection of melanoma: SSE–skin self-examination, PASE–partner-assisted skin examination, and CES–physician-led/clinical skin examination (secondary research question). We found inconsistent reporting across the included trials for all of the behavioural outcomes, reflected in many "unclear" ratings for the risk of bias assessment and a lack of pre-registration of study procedures, including analyses and assessment of outcomes. There was some variation between the trials with respect to intervention content and method of assessment for the behavioural outcomes. Of note, all of the outcomes were assessed using non-validated, mostly single-item measures. When comparing active interventions to non-active controls, we found small intervention effects for SSE, but not for PASE or CSE, when outcomes were assessed as binary (% of reported events). The combined sample sizes used in meta-analysis with SSE as outcome were large (n=817 active, n=828 control), but much smaller for the analyses with PASE and CSE due to fewer included studies. Also, there was evidence of publication bias, as per funnel plot analysis, which calls for cautious interpretation of our findings – as the pooled effect might not be generalizable beyond the studies examined here.

The results from the studies not included in our meta-analyses were reported individually and should also be interpreted with caution due to small sample sizes, which is problematic because it could lead to overestimation of intervention effects. For example, for continuous outcomes, a parallel 2-arm RCT with an 80%

power to detect a medium effect (Cohen d = 0.50) testing a two-tailed hypothesis with a critical alpha =0.05 requires at least 105 people per arm. To detect a small effect (Cohen d = 0.20) a trial would need at least 310 people per arm.

Our results are in line with findings from previous systematic reviews, which also did not identify any trials assessing mortality and early detection of melanoma and reported mixed results for the behavioural outcomes (Henrikson et al., 2018; Wu et al., 2016). Some of the trials included in our review were also included in the Wu (9) and the Henriksen (7) reviews. The current review is the most comprehensive review of behavioural prevention intervention RCTs with individuals at increased risk for melanoma to date.

Limitations and Directions for Future Research

The primary goal of a systematic review is to synthesize the existing literature, so that it is manageable and useful for clinicians and researchers. A secondary goal is to highlight strengths and weaknesses of the current literature and to point out gaps to be filled by future research. The main methodological issues identified by this review are limited sample sizes, use of different methods to assess the behavioural outcomes, and variability in terms of intervention content among prevention intervention RCTs with individuals at increased risk for melanoma. Despite the methodological issues, there are strengths in this body of work, primarily in the area of intervention development and the use of relevant outcomes for melanoma prevention/melanoma early detection (Ferris, 2018; Robinson & Halpern, 2016; Svoboda et al., 2018). However, there are no standardized measures available for the assessment of SSE and PASE (Coroiu et al., In Preparation). We used strict inclusion and exclusion criteria, as pre-specified in the PROSPERO registration, but added post hoc, two additional behavioural outcomes: a) partner-assisted skin examination, which is arguably a variant of SSE, but often reported as a separate outcome; and b) receiving a physician-led/ clinical skin exam (or CSE), which some of the included trials targeted through specific content included in the active interventions. Unfortunately, the trials assessing CSE did not track whether the exam was requested by the patient or initiated by the physicians, which is a limitation when it comes to interpreting the results pertaining to this outcome.

Moving forward, it is important to identify clear directions for future studies. First, trial registration is of crucial importance, which should include study design and hypotheses, outcomes (specifically differentiating

between primary and secondary outcomes, which directly relates to estimating power and sample size), and planned data analyses. Trial registration is not optional, in fact, as mandated by the International Committee of Medical Journal Editors (ICMJE) in 2005, it has been required for all clinical trials assessing medication effects (De Angelis et al., 2005; Zarin, Tse, Williams, & Carr, 2016). Behavioural trials, while currently lagging behind, could nonetheless benefit from adopting these recommendations as well (Riehm, Azar, & Thombs, 2015). However, most trial registration platforms do not have strict criteria for registration. Thus, in the absence of specific guidelines for trial registration, researchers have to hold themselves accountable to the scrutiny of the academic community by providing as much information as possible, which will allow for careful evaluation of design/analyses and planning of future replications. In addition to trial registration, it is good practice that detailed trial protocols be made available prior to commencement of recruitment: options include traditional publication via peer-reviewed articles and/ or the use of open access platforms, such as Open Science Foundation (OSF; https://osf.io/). In these lengthier documents, authors can specify the data analysis plan and the outcomes including how they will be scored. This will allow differentiating between post hoc analyses and a priori/pre-planned analyses. Second, behavioural trials involving skin cancer prevention strategies would benefit from improved reporting regarding recruitment and randomization procedures, group allocation, blinding (and decisions made in order to minimize the impact of no blinding of condition or blinding of the outcome assessment), and data analysis, including the management of attrition in analyses. In trial reports, post hoc decisions need to be clearly stated and justified as this allows for proper evaluation and replication. In addition, transparent reporting involves the reporting of all sensitivity analyses conducted, using appendices and /or open access repositories. Needless to say, it is of crucial importance that all analyses, regardless of significance or consistency with hypothesized magnitude and/or direction, should be reported in the trial report, so that future meta-analyses can take them into account. A CONSORT extension was recently developed to address issues specific to non-pharmacological trials, such as blinding procedures, group allocation, delays between randomization and initiation of treatment, and the provision of detailed information about the interventions (Boutron et al., 2017). Last, there is currently no standardized way of assessing SSE and PASE, which makes it difficult to draw conclusions across studies, i.e., synthesize the findings across studies. The melanoma

prevention field needs future research to establish the validity and reliability of scales assessing preventive behaviours, such as SSE and PASE. This would render the results from different studies comparable and potentially easier to combine in meta-analyses aiming to summarize the overall effect of interventions. Currently there is an ongoing team effort conducted through the COMET Initiative (Williamson & Clarke, 2012) to establish common norms (or "core outcome sets" [COS]) for the assessment of health and health-related quality of life outcomes in melanoma clinical trials. This project will inform future research by providing uniform guidelines for researchers to assess relevant outcomes in ways that makes comparison across trials possible (Prinsen et al., 2018). Regarding clinical skin exams, more reliable estimates may be derived from double-checking the self-report against medical records. For SSE and PASE, the use of technology (e.g., real-time tracking of SSE via smart-phone app) could improve the current methods of tracking, recording, and communicating to healthcare professionals about problematic lesions.

Conclusion

This is a comprehensive systematic review assessing the effect of prevention-focused interventions on melanoma-related mortality, melanoma early detection, and preventive behaviours previously hypothesized to facilitate early detection of melanoma, i.e., skin self-examination, partner-assisted skin examination, and physician-led clinical skin examination. No randomized controlled trials assessing mortality or early detection were identified. Twelve trials assessed one or all of the behavioural outcomes of interest. We identified a largely unclear risk of bias within the included studies and differing levels of heterogeneity between the studies. Therefore we conclude that the results of the existing trials on melanoma secondary prevention via early detection should be interpreted tentatively. Future research, with more rigorous trial design and improved reporting, is needed to determine the impact of behavioural interventions on health and health-related outcomes among those at increased risk for melanoma.

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Table 1. Characteristics of All 12 Trials Included in This Review

Trial	Funding Trial name Registration	Hypothesis, Trial design (Randomization unit)	Population (Risk factor)	Setting	Number/ group	Female n (%)	Age M ± SD or n (%)	Intervention	Control	Relevant outcomes
Bowen, 2015 United States	NIH: P20G007243 NCI: R01CA107430 Suntalk Study Unregistered	Comparative superiority Cluster RCT (2-arm, waitlist control) (family)	Melanoma patients (personal history)	Cancer registry	Intx 157 Ctrl 156	Total 175 (56)	Total 56.11 ± 12.33	Web-based communication and support	Waitlist	SSE, CSE
Geller, 2006 United States	NCI: R01CA76333 Unregistered	Comparative superiority Cluster RCT with longitudinal FU (2-arm, parallel) (family)	FDR (siblings) of melanoma patients (family history)	Hospital cancer center	Intx 237 Ctrl 257	Intx 123 (51.9) Ctrl 141 (54.9)	Reported > 51 Intx 105 (44.3) Ctrl 101 (39.4)	Tailored phone counselling	TAU	SSE, PASE, CSE
Glanz, 2010, United States	NCI: CA76419 Project SCAPE Unregistered	Comparative superiority Individual RCT (2 arm, parallel) (at-risk person)	At-risk outpatients (BRAT)	Primary care clinic	Intx 362 Ctrl 362	Intx 285 (78.7) Ctrl 276 (76.2)	Intx 42.1 ± 10.8 Ctrl 41.2 ± 11.2	Tailored intx	TAU	SSE
Glanz, 2013, United States	NIH #5UC2CA148310-02 GenoMEL Unregistered	Comparative superiority Cluster RCT (2-arm, parallel) (family)	At-risk outpatients (personal and family history)[a]	Pigmented lesion clinic	Intx 35 Ctrl 38	Intx 28 (80.0) Ctrl 22 (57.9)	Intx 62.4 ± 14.6 Ctrl 56.9 ± 16.1	Genetic counselling	TAU	SSE, CSE
Glanz, 2015, United States	NIH #5UC2CA148310 PennSCAPE trial NCT01356771	Comparative superiority Individual RCT (2-arm, parallel) (at-risk person)	At-risk outpatients (BRAT)	Primary care clinic	Intx 95 Ctrl 111	Completers: Intx 62 (74.7) Ctrl 79 (72.5)	Completers Intx 53.5 ± 14.4 Ctrl 56.5 ± 15.7	Tailored mailing	TAU	SSE, CSE

Trial	Funding Trial name Registration	Hypothesis, Trial design (Randomization unit)	Population (Risk factor)	Setting	Number/ group	Female n (%)	Age M ± SD or n (%)	Intervention	Control	Relevant outcomes
Glazebrook, 2006, United Kingdom	Trent NHS Skinsafe trial Unregistered	Comparative superiority Cluster RCT (2 arm, parallel) (clinic)	At-risk outpatients[b] (phenotype, personal history)	Primary care clinic	Intx 259 Ctrl 330	Intx 214 (82.6) Ctrl 259 (78.5)	Intx38.2 ± 14.3 Ctrl38.4 ± 15.2	Health education via computer program	TAU	SSE
Manne, 2010, United States	NCI #5R01 CA107312-02 & CA006927 NCT00816374	Comparative superiority Cluster RCT w/ longitudinal FU (2-arm, parallel) (family)	FDR of melanoma patients family history)	Skin cancer clinic	Intx 225 Ctrl 218	Intx 135 (60.0) Ctrl 144 (66.1)	Intx 48.1 ± 12.6 Ctrl 47.1 ± 13.9	Tailored print and phone counseling	Generic print and phone counselling	SSE, CSE
Oliveria, 2004, United States	No funding reported Unregistered	Comparative superiority Individual RCT (2 arm parallel) (at-risk person)	At-risk outpatients (>=5 clinical dysplastic/ atypical nevi)	Pigmented lesion clinic	Intx 49 Ctrl 51	Intx 29 (59.2) Ctrl 34 (66.7)	Intx 40.3 ± 10.9 Ctrl 39.4 ± 11.5	Teaching with photobook	Teaching without photobook	SSE
Rat, 2014, France	French National Institute of Cancer COPARIME project NCT01610531	Comparative superiority Pilot Cluster RCT (2-arm, parallel) (GPs)	At-risk outpatients (SAMScore)	Primary care clinic	Intx 97 Ctrl 76	Intx: 74 (76) Ctrl: 58 (76)	Intx 43.6 ± 17.1 Ctrl 42.8 ± 14.6	Targeted screening and education	TAU	SSE
Robinson, 2007, United States	NCI #5R21 CA-103833-02 NCT01013844	Comparative superiority Individual RCT w/ longitudinal FU (2-arm parallel) (patient)	Melanoma patients (personal history)	Melanoma/ Hospital registry	Intx 65 Ctrl 65	Intx: 33 (51) Ctrl: 32 (49)	Median Intx 40-49 Ctrl 50-59	Dyadic learning	Solo learning	SSE, PASE

Trial	Funding Trial name Registration	Hypothesis, Trial design (Randomization unit)	Population (Risk factor)	Setting	Number/ group	Female n (%)	Age M ± SD or n (%)	Intervention	Control	Relevant outcomes
Robinson, 2010, United States	NCI #5R21 CA-103833-02 Unregistered *(Declared as Pilot for Turrisi, 2015)*	Comparative, superiority/ non-inferiority Individual RCT w/ longitudinal FU (2-arm parallel) (patient)	Melanoma patients (personal history)	Not reported	Intx 21 Ctrl 19	Intx: 10 (53) Ctrl: 11 (52)	Median Intx 40-49 Control: 40-49	Workbook	In-person	PASE
Turrisi, 2015, United States	NCI #R01-CA154908 NCT01432860	Superiority and equivalency/ noninferiority Multiple Arm RCT w/ longitudinal FU (4-arm parallel) (patient)	Melanoma patients (personal history)	Medical records, News-papers	In-person 165 Workbook 159 Tablet 71 Ctrl 99	In person 75 (45.5) Workbook 81 (50.9) Tablet 37 (52.1) Ctrl 60 (60.6)	Median In-person 50-59 Workbook 50-59 Tablet 50-59 Ctrl 50-59	In-person vs. Workbook vs. Tablet	TAU	PASE

Note. GP = General practitioner; Intx=intervention, CTRL=control; SSE = skin self-examination; PASE = partner-assisted skin examination; CSE = clinical skin exam; FDR = first degree relative; BRAT = Brief *Skin Cancer* Risk Assessment Tool; risk scores: moderate (27-35) and high risk (>35) included; SAMScore = Self-Assessment of Melanoma Risk Score; high risk assessed based on the following criteria (a) at least 3 risk factors: skin type, sun burns, living location, melanoma history; (b) < 60 year old + > 20 nevi on the arms, or (c) > 60 yo + freckles); [a] Family member = 3+ cases of melanoma on the same side of family OR 2 + cases of melanoma in FDRs). [b] Red hair, multiple moles, history of sunburns as a child, freckling, family history of melanoma, fair sun-sensitive skin.

Table 2. Risk of Bias Assessment for Individually Randomized Trials

Trial	Sequence generation	Allocation sequence concealment	Blinding of participants	Blinding of personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting of outcomes	Other
Glanz, 2010 (Glanz et al., 2010)	Unclear	Unclear	Low	Low	Low	Unclear	Unclear	Unclear
Glanz, 2015 (Glanz et al., 2015)	Low	Unclear	Low	Low	Low	Unclear	Unclear (for both outcomes)	Unclear
Oliveria, 2004 (Oliveria et al., 2004)	Unclear	Unclear	Unclear	Unclear	Low	Unclear	Unclear	Unclear
Robinson, 2007 (Robinson et al., 2007a)	Unclear	Unclear	Low	Low	Low	Low	Unclear (for both outcomes)	Unclear
Robinson, 2010 (Robinson et al., 2010)	Unclear	Unclear	Low	Low	Low	Unclear	Unclear	Unclear
Turrisi, 2015 (Turrisi et al., 2015)	Unclear	Unclear	Unclear	Unclear	Low	Unclear	Unclear	Unclear

Table 3. Risk of Bias Assessment for Cluster Randomized Trials

Trial	Recruitment bias	Baseline imbalance	Loss of clusters	Incorrect statistical methods	Comparability with individually randomized trials
Bowen, 2015 (Bowen et al., 2015)	Low	Unclear	Unclear	High	Low
Geller, 2006 (Geller et al., 2006)	Low	Low	Unclear	Low	Low
Glanz, 2013 (Glanz et al., 2013)	Low	Unclear	Unclear	Low	Low
Glazebrook, 2006 (Glazebrook et al., 2006)	Unclear	Low	Unclear	Low	Low
Manne, 2010 (Manne et al., 2010)	Unclear	Unclear	Unclear	SSE High CSE Low	SSE Low, CSE Low
Rat, 2014 (Rat et al., 2014)	Unclear	Unclear	Low	Low	Low

Note. SSE = skin self-examination; CSE = clinical skin exam.

Table 4. Heterogeneity Assessment for Trials Comparing an Active Intervention to a Non-Active Control

Trial	Intervention components				Intervention duration	Non-active control	Outcome/ Measure of effect	Follow-up (post intx)
	Info	Skills	Psych	Med				
Bowen, 2015* (Bowen et al., 2015)	Website Tailored prevention info	-	-	-	12 months	Waitlist	SSE of specific areas (%) At least 1x SSE [body part] in the last 2 months SSE (%) At least 1x thorough SSE in the last 2 months CSE (%) At least 1x CSE in the last 2 months	12 months
Glanz, 2010 (Glanz et al., 2010)	Pamphlet (x3) Tailored prevention info	-	-	-	-	TAU	SSE (%) At least 1x SSE in the last 3 months	3 months
Glazebrook, 2006* (Glazebrook et al., 2006)	Computer program Tailored prevention info	-	-	-	10-15 min	TAU	SSE (%) At least 1x SSE in the last 6 months PASE (%) At least 1x PASE in the last 6 months	6 months
Rat, 2014* (Rat et al., 2014)	Pamphlet Generic prevention info	-	-	CSE CSE and tailored feedback on risk	Duration of GP session not reported	TAU	SSE (%) At least 1x SSE in the last 12 months PASE (%) At least 1x PASE in the last 12 months SSE w/ own photograph (%) At least 1x SSE w/ photos in the last 12 months	5 months
Geller, 2006* (Geller et al., 2006)	Pamphlet (x3) Tailored prevention info	-	Counselling sessions (x4) Goal-setting for behaviour change; Barriers to SSE and CSE	-	10-15 min/ session (intx delivered over > 5 months)	TAU	SSE (%) At least 1x SSE (checking all moles) in the last 12 months SSE w/ mole comparison (%) At least 1x SSE (comparing all moles) in the last 12 months PASE (%) At least 1x PASE in the last 12 months	1, 6 months (6, 12 months post baseline)

Trial	Intervention components				Intervention duration	Non-active control	Outcome/ Measure of effect	Follow-up (post intx)
	Info	Skills	Psych	Med				
							SSE w/ picture (%) At least 1x SSE (using pic to compare moles) in the last 12 months CSE (%) At least 1x CSE in the last 12 months	
Glanz, 2015 (Glanz et al., 2015)	Pamphlet (x3) Tailored prevention info	-	-		-	TAU	SSE (M/SD) Recency of last SSE ("never" to "last month") 1=never 4=last month CSE (M/SD) Frequency of CSE in last 3 months 0=never 4= each month or more	3 months
Glanz, 2013* (Glanz et al., 2013)	Pamphlet Generic prevention info	-	-	Genetic counselling session With test results and referrals	45-60 min	TAU	SSE (M/SD) Recency of last thorough SSE ("never" to "last month") 1=within past month 4=never CSE (M/SD) Frequency of CSE during last 4 months Range not reported	4 months
Turrisi, 2015[a] (Turrisi et al., 2015)	Pamphlet Generic prevention info	ABCDE criteria SSE kit; SSE accuracy quiz	-	CSE (x3) CSE and mole-tracking demo	30 min	TAU	PASE (M/SD) Frequency of PASE in the last 4 months ("never" to "daily") 0=never 4=4 times or more	4, 12 months
Turrisi, 2015[b] (Turrisi et al., 2015)	Workbook Generic prevention info	ABCDE criteria SSE kit; SSE accuracy quiz	-	CSE (x3) CSE and mole-tracking demo	24 min	TAU	PASE (M/SD) Frequency of PASE in the last 4 months ("never" to "daily") 0=never 4=4 times or more	4, 12 months

Trial	Intervention components				Intervention duration	Non-active control	Outcome/ Measure of effect	Follow-up (post intx)
	Info	Skills	Psych	Med				
Turrisi, 2015[c] (Turrisi et al., 2015)	Tablet Generic prevention info	ABCDE criteria SSE kit; SSE accuracy quiz	-	CSE (x3) CSE and mole-tracking demo	30 min	TAU	PASE (M/SD) Frequency of PASE in the last 4 months ("never" to "daily") 0=never 4=4 times or more	4, 12 months

Note. SSE = skin self-exam, PASE = partner-assisted skin exam, CSE = clinical skin exam, Intx = intervention.
Info = passive delivery of melanoma prevention information, including behaviours targeting melanoma early detection (e.g, skin exams).
Skills = demonstration of how to check the skin for problematic lesions (including teaching session, practical exercises) and how to ask for clinical skin exams.
Psych = use of psychological/psychotherapy techniques (guided imagery, motivational interviewing) to address individual-level barriers to screening.
Med = physician-led clinical skin exams (CSE) and genetic counselling.
* Cluster randomized controlled trial.
[a] Comparison for in-person intervention against TAU.
[b] Comparison for workbook intervention against TAU.
[c] Comparison for tablet intervention against TAU.

Table 5. Heterogeneity Assessment for Trials Comparing an Active Intervention to an Active Control

Trial	Intervention					Active comparator					Outcome (measure of effect)	Follow-up assessments
	Info	Skills	Psych	Med	Duration	Info	Skills	Psych	Med	Duration		
Manne, 2010* (Manne et al., 2010)	Pamphlet (x3) Tailored prevention info	ABCDE criteria SSE demo; asking for CSE	Counselling session Personal risk, barriers to SSE and CSE	-	30 min	Pamphlet (x3) Generic prevention info	ABCDE criteria CSE SSE demo; asking for CSE	- Generic, info session for controls	-	12 min	SSE (M/SD) Frequency of SSE in the last 3 months Range not reported CSE (%) At least 1x CSE in the last 3 (9) months	3, 9 months
Oliveria, 2004 (Oliveria et al., 2004)	Pamphlet, Video, Photographs Generic prevention info; full body photographs	ABCDE criteria SSE demo w/ photographs; SSE exercises	Counselling session Guided imagery /relaxation	-	2 hours	Pamphlet Video Generic prevention info	ABCDE criteria SSE demo w/ mole map; SSE exercises	Counselling session Guided imagery /relaxation	-	60 min	SSE (%) At least 3x SSE in the last 4 months	4 months
Robinson, 2007 (Robinson et al., 2007)	Pamphlet to dyad Generic prevention info	ABCDE criteria to dyad SSE kit; SSE demo; SSE quiz	-	-	10 min	Pamphlet to patient Generic prevention info	ABCDE criteria to patient SSE kit; SSE demo; SSE quiz	-	-	10 min	SSE (M/SD) Frequency of SSE in the last 4 months ("never" to "daily") 0 = Never 4 = Daily PASE (M/SD) Frequency of PASE in the last 4 months ("never" to "daily")	4 months
Robinson, 2010 (Robinson et al., 2010)	Workbook to dyad Generic prevention info	ABCDE criteria to dyad SSE kit; SSE exercises	-	-	-	In person to patient Generic prevention info	ABCDE criteria to patient SSE kit; SSE demo	-	-	15 min	PASE (M/SD) Frequency of PASE in the last 4 months ("never" to "daily") 0 = Never 4 = Daily	1, 4 months

Trial	Intervention					Active comparator					Outcome (measure of effect)	Follow-up assessments
	Info	Skills	Psych	Med	Duration	Info	Skills	Psych	Med	Duration		
Turrisi, 2015 [a] (Turrisi et al., 2015)	Workbook Generic prevention info	ABCDE criteria SSE kit; SSE accuracy quiz	-	CSE (x3) CSE and mole-tracking demo	24 min	Pamphlet Generic prevention info	ABCDE criteria SSE kit; SSE accuracy quiz	-	CSE (x3) CSE and mole-tracking demo	30 min	PASE (M/SD) Frequency of PASE in the last 4 months ("never" to "daily") 0 = never 4 = 4 PASE or more	4, 12 months
Turrisi, 2015 [b] (Turrisi et al., 2015)	Tablet Generic prevention info	ABCDE criteria SSE kit; SSE accuracy quiz	-	CSE (x3) CSE and mole-tracking demo	30 min	Pamphlet Generic prevention info	ABCDE criteria SSE kit; SSE accuracy quiz	-	CSE (x3) CSE and mole-tracking demo	30 min	PASE (M/SD) Frequency of PASE in the last 4 months ("never" to "daily") 0 = never 4 = 4 PASE or more	4, 12 months

Note. SSE = skin self-exam, PASE = partner-assisted skin exam, CSE = clinical skin exam.
Info = passive delivery of melanoma prevention information, including behaviours targeting melanoma early detection (skin exams).
Skills = demonstration of how to check the skin for problematic lesions (including teaching session, practical exercises) and how to ask for clinical skin exams.
Psych = use of psychological/psychotherapy techniques (guided imagery, motivational interviewing) to address individual-level barriers to screening.
Med = physician-led clinical skin exams (CSE) and genetic counselling.
* Cluster randomized controlled trial.
[a] Comparison for workbook intervention against in-person intervention.
[b] Comparison for tablet intervention against in-person intervention.

PRISMA FLOWCHART

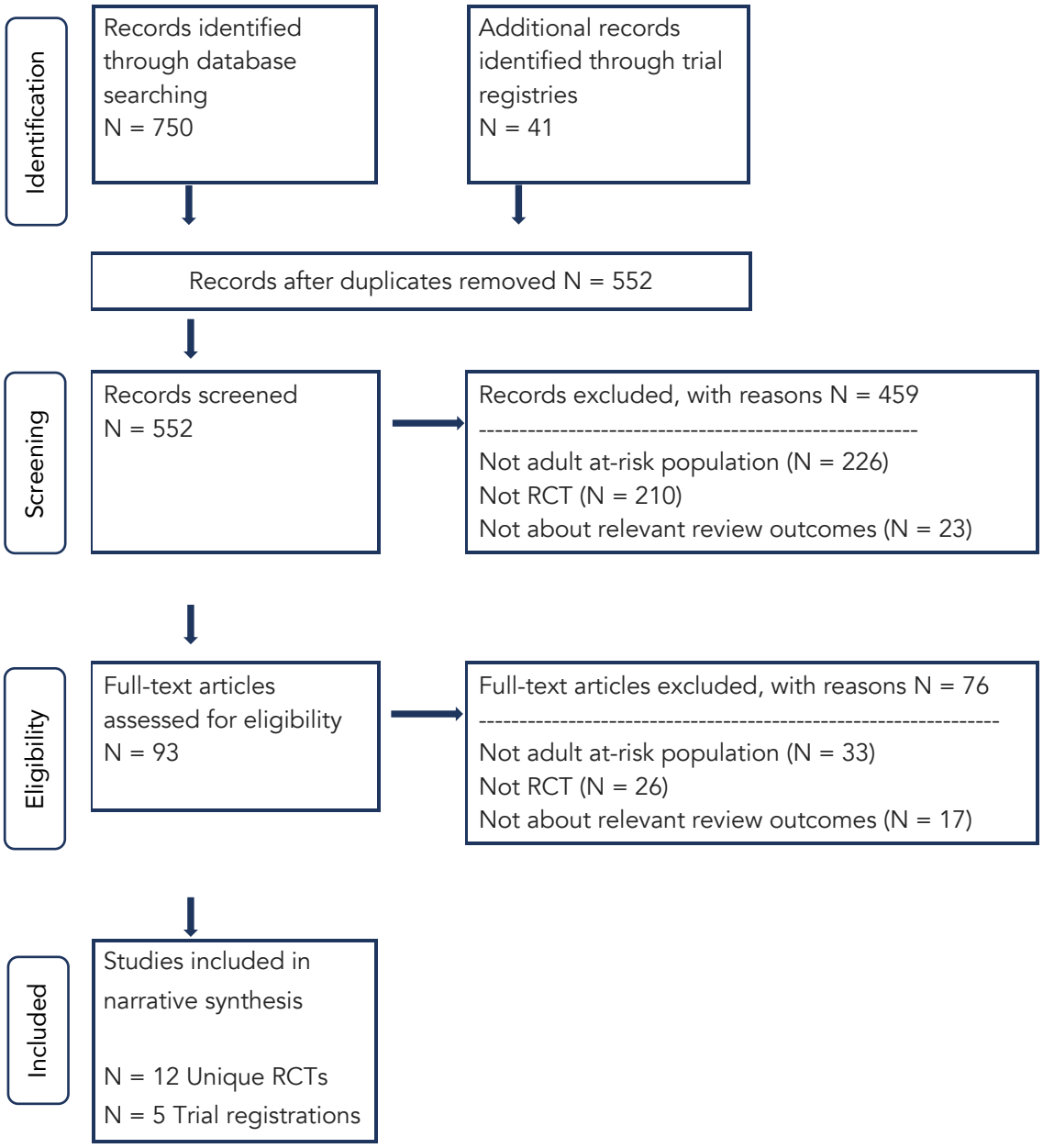

Figure 1. PRISMA flowchart of study selection.
Adapted from Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., & and the Prisma Group. (2009). Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. Annals of Internal Medicine, 151(4), 264-269. doi:10.7326/0003-4819-151-4-200908180-00135.

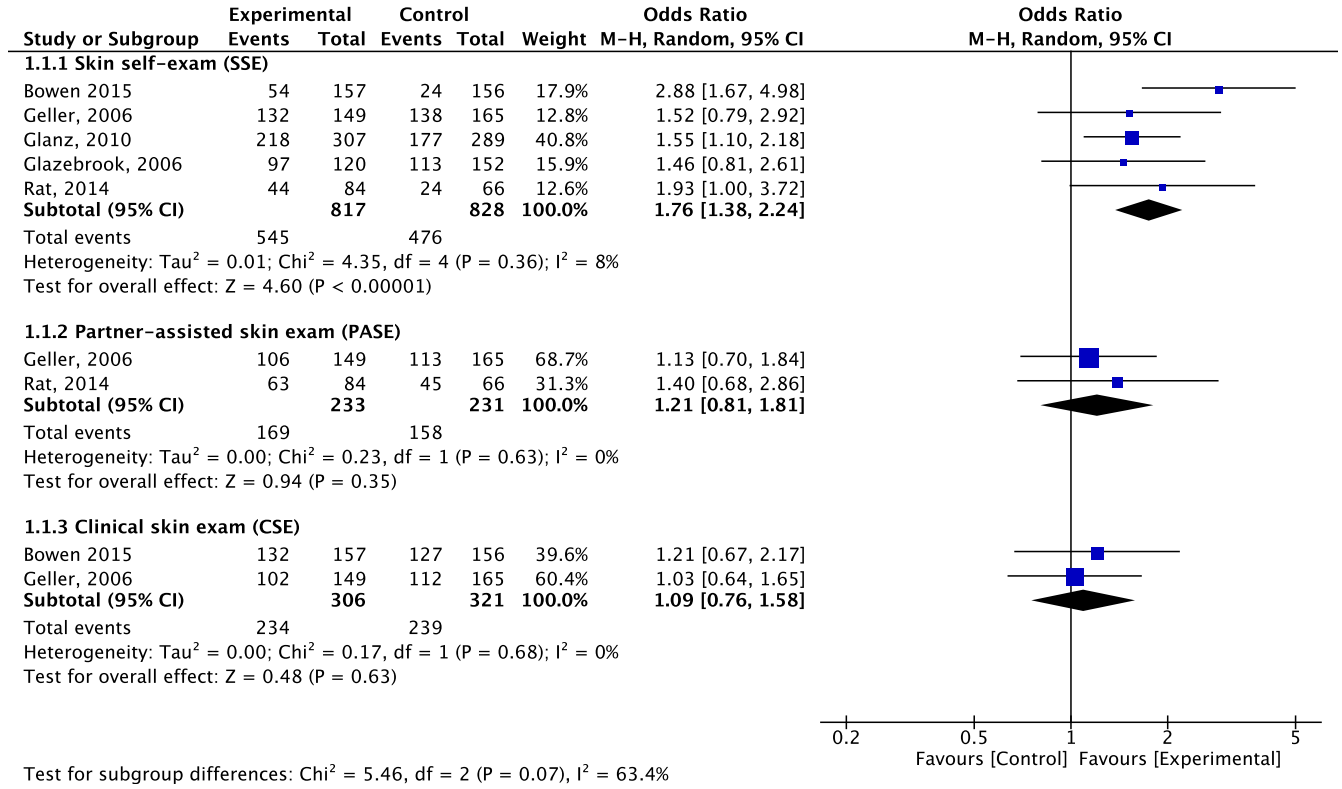

Figure 2. Forrest plot with studies comparing an intervention versus a non-active comparator with behavioural outcomes measured as proportions.

Note. The sample sizes and the proportions of endorsed events were adjusted by the design (cluster) effect for Bowen, Geller, Glazebrook, and Rat trials.

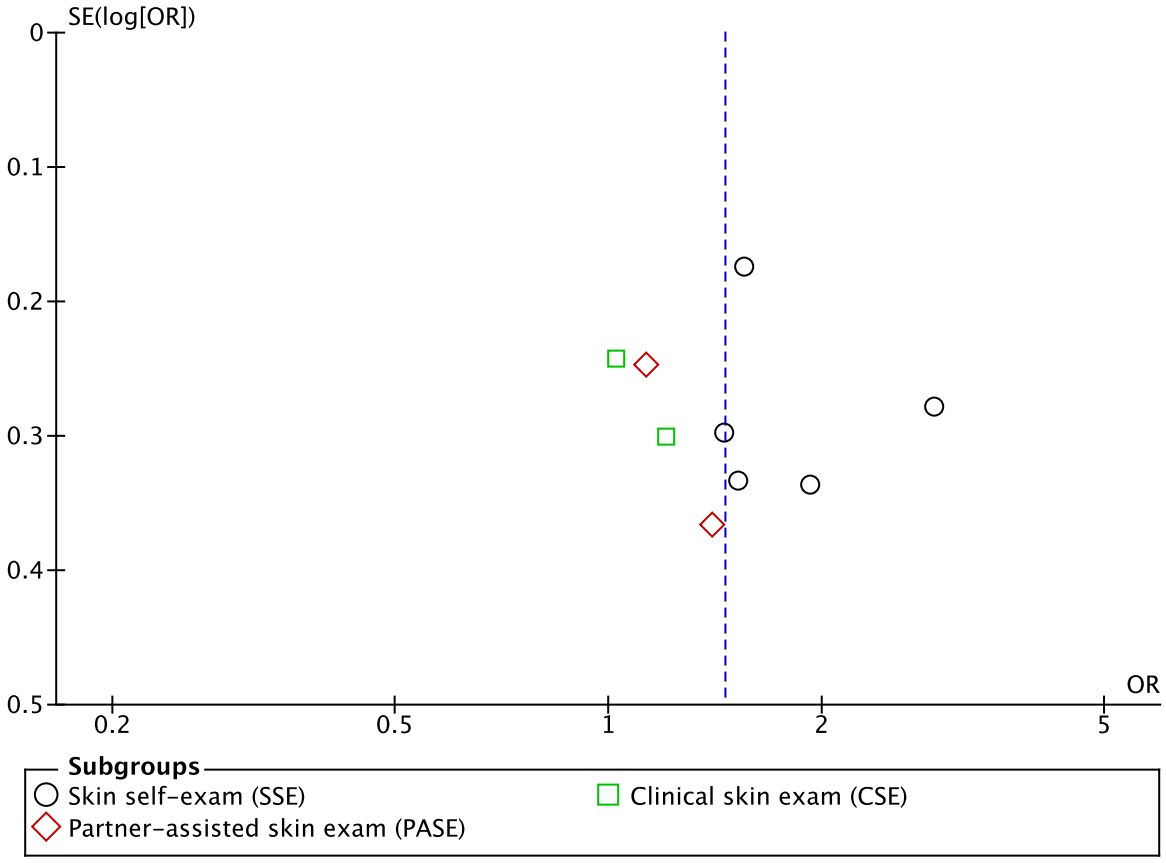

Figure 3. Funnel Plot with studies comparing an intervention versus a non-active comparator with behavioural outcomes measured as proportions.

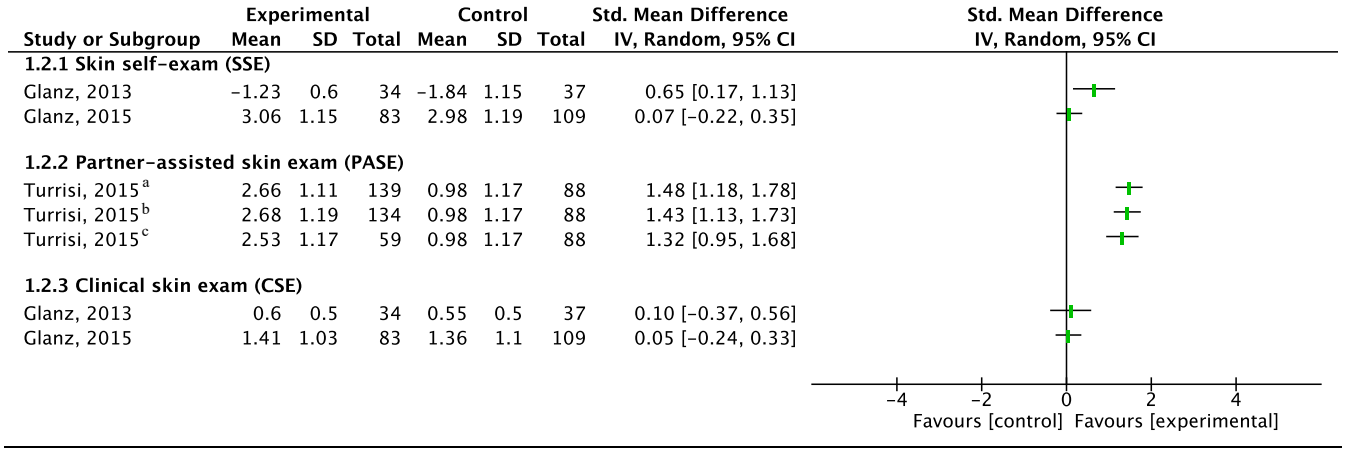

Figure 4. Forrest plot with studies comparing an intervention versus a non-active comparator with behavioural outcomes measured as continuous variables.

Note. The sample size was adjusted by the design (cluster) effect for the Glanz 2013 trial.

[a] In-person intervention versus control.

[b] Workbook intervention versus control.

[c] Tablet intervention versus control.

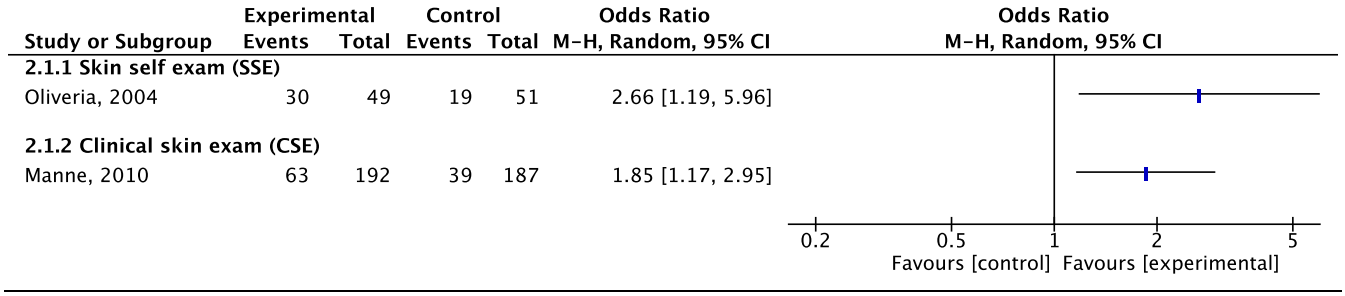

Figure 5. Forrest plot with studies comparing an intervention versus an active comparator with behavioural outcomes measured as proportions.
Note. The sample size was adjusted by the design (cluster) effect for the Manne 2010 trial.

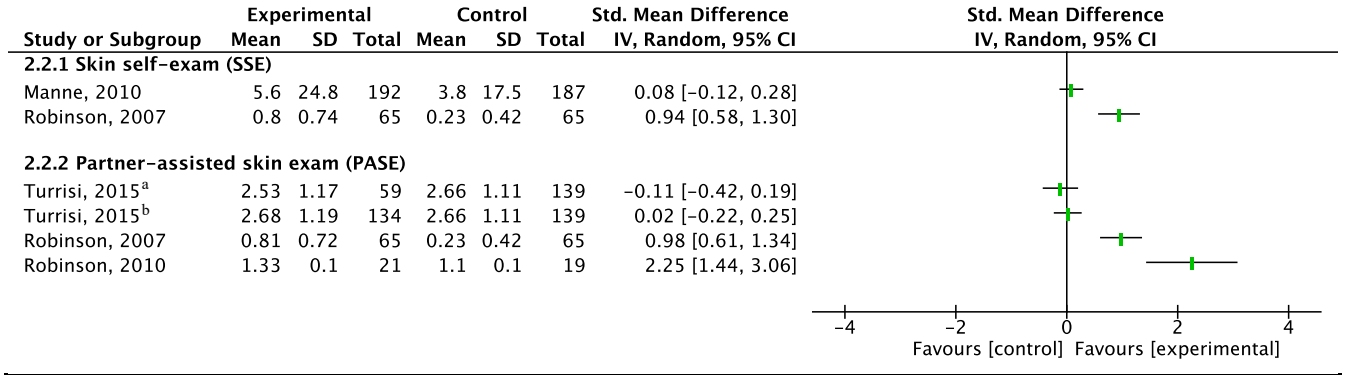

Figure 6. Forrest plot with studies comparing active intervention versus active control on continuous outcomes
Note. The sample size was adjusted by the design (cluster) effect for the Manne 2010 trial.
[a] Tablet intervention versus In-person intervention.
[b] Workbook intervention versus In-person intervention.

Appendix 1: Medline Search

Medline
Database(s): Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily, Ovid MEDLINE(R) and Ovid OLDMEDLINE(R) 1946 to Present
Search Strategy:

#	Searches	Results
1	Melanoma/ or melanoma.mp.	102432
2	self examination.mp. or Self-Examination/	3558
3	self exam*.mp.	3707
4	self screen*.mp.	151
5	self surveillance.mp.	57
6	self monitor*.mp.	8813
7	skin exam*.mp.	769
8	2 or 3 or 4 or 5 or 6 or 7	13364
9	skin neoplasms.mp. or Skin Neoplasms/	101285
10	skin cancer.mp.	13147
11	skin surveillance.mp.	41
12	8 or 11	13396
13	1 or 9 or 10	174715
14	12 and 13	766
15	randomized controlled trial.pt.	404274
16	controlled clinical trial.pt.	89994
17	randomi?ed.ab.	397618
18	placebo.ab.	165263
19	drug therapy.fs.	1810175
20	randomly.ab.	240295
21	trial.ab.	343550
22	groups.ab.	1504295
23	or/15-22	3643127
24	exp animals/ not humans.sh.	4173179
25	23 not 24	3133238
26	14 and 25	187

Appendix 2: Inclusion Criteria

Inclusion	Exclusion
(P) Population: • Individuals at increased risk for melanoma • Adults (18+) Increased Risk (environmental +bio factors): • Immunosuppressed individuals (radiation; transplant) • History of childhood radiation • Melanoma patients • People w/ a history of melanoma • Non-melanoma skin cancer (NMSC, i.e., BCC/SCC) patients • 100+ naevi (moles; birth or beauty marks) or 5+ atypical naevi • First degree relatives of melanoma patients • 50-100 naevi • 1+ atypical naevi (http://www.dermnetnz.org/lesions/atypical-naevi.html) • Phenotypic features ▪ red or blond hair ▪ tendency to freckle ▪ gets easily burnt ▪ tanned skin	• General Population • Children/youth below 18 • Men 50+ • Spouses and other non-blood relatives of melanoma patients Other examples of non-eligible groups: • Beach-goers • University/college students • Patients presenting for routine medical visits • Healthcare professionals working in melanoma clinics • Parents of children treated for childhood cancers
(I) Intervention: • Design: Randomized controlled trial, with min two groups • Content: Any Informational, educational, psychological, didactic intervention	• Design: Not an RCT Content: Medical procedures (pharmacological, surgery/biopsy)
(C) Comparison: • at least one other intervention or control arm	
(O) Outcomes: • SSE behaviour • Early detection • Mortality	• SSE not an outcome • SSE Accuracy as outcome (i.e., identifying problematic lesions accurately via SSE) • Any other outcomes
Language: • English, French, German, Spanish, Russian, Romanian	• Any other language

Note. NMSC = non-melanoma skin cancer; BCC= basal cell carcinoma; SCC= squamous cell melanoma.

Appendix 3: Data Coding Sheet for Titles and Abstracts and Full Text Screening

Refid: 1, There and Back Again: A Review of Residency and Return Migrations in Sharks, with Implications for Population Structure and Management. Chapman DD, Feldheim KA, Papastamatiou Y, Hueter RE

The overexploitation of sharks has become a global environmental issue in need of a comprehensive and multifaceted management response. Tracking studies are beginning to elucidate how shark movements shape the internal dynamics and structure of populations, which determine the most appropriate scale of these management efforts.

Tracked sharks frequently either remain in a restricted geographic area for an extended period of time (residency) or return to a previously resided-in area after making long-distance movements (site fidelity). Genetic studies have shown that some individuals of certain species preferentially return to their exact birthplaces (natal philopatry) or birth regions (regional philopatry) for either parturition or mating, even though they make long-distance movements that would allow them to breed elsewhere. More than 80 peer-reviewed articles, constituting the majority of published shark tracking and population genetic studies, provide evidence of at least one of these behaviors in a combined 31 shark species from six of the eight extant orders.

Residency, site fidelity, and philopatry can alone or in combination structure many coastal shark populations on finer geographic scales than expected based on their potential for dispersal. This information should therefore be used to scale and inform assessment, management, and conservation activities intended to restore depleted shark populations. Expected final online publication date for the Annual Review of Marine Science Volume 7 is January 03, 2015.

1. **Population: Adults at High Risk for Melanoma?**
   - ◯ Yes
   - ◯ No
   - ◯ Maybe

2. **Intervention: RCT** (educational, informational, psychosocial)**?**

   If study uses data from a trial => include
   - ◯ Yes
   - ◯ No
   - ◯ Maybe

3. **Outcome: SSE (Skin self-examination)?**
   - ◯ Yes
   - ◯ No
   - ◯ Maybe

4. **Outcome: Early Detection (melanoma size, depth; melanoma stage)?**
   - ◯ Yes
   - ◯ No
   - ◯ Maybe

   Clear Response ()

5. **Outcome: Mortality or Survival?**
   - ◯ Yes
   - ◯ No
   - ◯ Maybe

   Clear Response ()

6. **Language: English, French, German (Spanish or Romanian)?**
   - ◯ Yes
   - ◯ No

Link Between Manuscripts 2 and 3

Manuscript 2 addressed an important question, i.e., whether there were efficacious interventions that promoted health (mortality, early detection) and health behaviours (e.g., SSE) among individuals at increased risk for melanoma. We were interested to see if there were benefits for people exposed to behavioural interventions that targeted SSE with respect to three types of outcomes. Yet, our review identified no behavioural trials that investigated mortality or early detection of melanoma. All of the 12 trials included in the review investigated melanoma preventive behaviours, including SSE[2], PASE[3], and CSE[4]. Manuscript 2 includes detailed information about the characteristics of the interventions that were found to be efficacious at promoting SSE and provides a synthesis of all existing prevention interventions conducted to date with individuals at increased risk. Data from Manuscript 1 was used to assess the methodological heterogeneity (i.e., variability in the methods of assessing SSE across the included trials). Overall, the evidence provided by manuscript 2 can inform public health policy about the efficacy of various modalities to promote SSE in at-risk groups.

Manuscript 3 is an empirical investigation of short- and long-term predictors of SSE behaviour in a sample of melanoma patients who received an educational session on how to perform SSE to identify problematic lesions. Manuscript 3 adds a nuanced understanding to the findings presented in Manuscript 2, by examining the variables that contribute to the long-term adherence of SSE. The issue of long-term adherence to medical regimens is best examined via observational, cohort studies, as efficacy RCT's are typically conducted over brief periods of time, and therefore less likely to match real-life scenarios. Manuscript 3 includes results from an observational study with longitudinal follow-up (3 assessment points, at 3, 12, and 24 months post an educational session on SSE) and aims to identify the strongest predictors of SSE behaviour,

[2] SSE = skin self-examination;
[3] PASE = partner-assisted skin examination
[4] CSE = clinician-administered skin exam

which may inform public health campaigns targeting individuals at increased risk for melanoma, alongside the findings from Manuscript 2.

Manuscript 3: Barriers and Facilitators of Skin Self-Examination Among Individuals in Melanoma Follow-up Care

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Authors' Contribution:

AC, A Körner Designed the study.

AC, A Kezouh Conducted data analysis.

AC, A Körner conducted the interpretation of data analysis.

CM, CB Assisted with the writing of the method section and formatting of tables with results.

AC completed the first draft of the manuscript.

CM, CB, MD, AG, GB, AK, AK Contributed critical feedback to earlier drafts for the manuscript, reviewed, and approved the final draft of the manuscript.

All authors read and approved the final draft of the manuscript.

Abstract

Background

Melanoma, the deadliest and fastest growing skin cancer, has high survival rates if detected early and treated. Further, melanoma survivors face a life-long risk of reoccurrence. Early detection of melanoma can be facilitated via skin self-examination (SSE) and as such, SSE is part of melanoma follow-up care. However, survivors' adherence to SSE is low. The main objective of this study is to identify short- and long-term predictors of SSE after providing best-practice clinical care, which includes medical advice on SSE.

Method

This is an observational study with longitudinal follow-up conducted with melanoma patients. Socio-demographic and medical variables as well as psychosocial variables (e.g., attitudes, intentions, and self-efficacy about SSE, distress, coping, physician support) were collected at 3 months post a standardized educational session on preventive behaviours. Outcome variables, SSE comprehensive (extent of body covered by the skin exam) and SSE optimal (monthly checking of entire body) were collected at 3, 12, and 24 months post the educational session. Hierarchical linear models examined the association between predictor variables and SSE comprehensive and logistic regressions examined the association between potential predictors and SSE optimal.

Results

Mean of SSE comprehensive and rates of SSE optimal were higher at three months after an educational session on SSE compared to 12 and 24 months post the education. In the short (3 months) and long-term (24 months), intentions to perform SSE consistently predicted SSE comprehensive and self-efficacy for SSE predicted adherence to optimal SSE. Other variables associated with SSE comprehensive at various follow-up points include biological sex (male), attitudes about SSE, and coping strategies. Other variables predicting SSE optimal at various follow-up points include SSE intentions, SSE attitudes, coping strategies, and physician support of SSE. Medical characteristics, other socio-demographic variables than sex, and melanoma knowledge were not associated with SSE.

Conclusions

This is the first studies in the literature to address the short (3 months) and long-term (12 and 24 months) predictors of SSE behaviour in a sample of melanoma patients receiving ongoing follow-up care. The strongest predictors of SSE found in our study, intentions to perform SSE and self-efficacy for SSE, are highly amenable to change and could be easily targeted in interventions aiming at the secondary prevention of melanoma.

Short and Long-term Barriers and Facilitators of SSE Among Individuals with Melanoma

Skin cancers are the most commonly diagnosed cancers in Canada and the United States (Erdei & Torres, 2010; Linos, Swetter, Cockburn, Colditz, & Clarke, 2009; Rogers, Weinstock, Feldman, & Coldiron, 2015). In 2018, there will be 91,270 new cases and 9,320 deaths from melanoma in the US (Howlader et al., 2016). In Canada, of the total numbers of new cancer cases in 2015 (100,00 males, 96, 400 females), 3.6 % in males and 3.2 % in females were melanomas (Canadian Cancer Society, 2015). Also, in 2015 there were 6800 new cases and 1150 deaths from melanoma in Canada. Melanoma tumours grow faster than other tumours and can metastasize when they are only 1 mm in depth (Safarians, Sternlight, Freiman, Huaman, & Barsky, 1996; Yang et al., 2009). Tumour thickness (Lambert & Lambert) at diagnosis is the best predictor of survival (Baade et al., 2006; Balch et al., 2009; Balch et al., 2001; Eisemann et al., 2012; Green, Baade, Coory, Aitken, & Smithers, 2012). Thus, early detection and timely treatment, i.e., surgical excision of the tumour are crucial to survival. The 5-year survival rate is excellent (98.4%) for patients diagnosed with localized disease (stages 0-II), but only 22.5% for distant disease (stages III-IV) (Howlader et al., 2016). A personal history of melanoma is associated with a life-long elevated risk for developing subsequent melanomas (Burdern et al., 1994; Geller, Swetter, Brooks, Demierre, & Yaroch, 2007; Uliasz & Lebwohl, 2007). Melanoma survivors have a 9-fold increased risk to develop subsequent melanomas compared to the general population (range= 12.6 to 26.4-fold) and the risk remains elevated 20 years past the initial diagnosis (Bradford, Freedman, Goldstein, & Tucker, 2010; van der Leest et al., 2012). 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).

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 pre-metastatic tumours (Geller, Swetter, & Weinstock, 2015; Rhodes, 2006); and that 2) intervention strategies will have the highest impact if targeting high-risk individuals (Garbe et al., 2003; Geller et al., 2007; Markovic et al., 2007; Rhodes, 2006; Weinstock, 2006). Because melanoma develops with a visible, pre-clinical phase, it is amenable to early detection via visual

inspection of the skin, by physicians and lay persons (Friedman, Rigel, & Kopf, 1985). Evidence-based clinical guidelines for melanoma follow-up and care developed in the United Kingdom recommend that melanoma patients should be a) given a full body skin exam (with palpation of the lymph nodes) at every follow-up appointment, b) given information (written and verbal) about types of skin cancer and instructions on skin self-examination (National Institute for Health and Care Excellence [NICE], 2015).

Clinical skin exams performed by physicians have been associated with thinner tumours at diagnosis (De Giorgi et al., 2012; Dessinioti et al., 2018; Pollitt et al., 2009; Swetter, Pollitt, Johnson, Brooks, & Geller, 2012) and a 14% reduced risk of thick tumours, which frequently indicate advanced disease (Aitken, Elwood, Baade, Youl, & English, 2010). While clinical exams are undoubtedly useful for the early identification of cancerous skin lesions, most dermatological and cancer associations (American Academy of Dermatology, 2018; American Cancer Society, 2015; National Comprehensive Cancer Network, 2018) as well as most clinical guidelines for the prevention of melanoma (Marciano, Merlin, Bessen, & Street, 2014; Watts et al., 2015) recommend that individuals at increased risk perform regular skin self-exams (SSE) in between medical follow-ups and present for medical skin exam if suspicious lesions are identified during skin self-exams.

Skin Self-Examination (SSE)

There is evidence that the practice of SSE is beneficial for high-risk individuals. Empirical cross-sectional studies have found that patients and family members detected up to 50-80% of all melanomas (Carli, De Giorgi, Betti, et al., 2003; De Giorgi et al., 2012; Swetter et al., 2012). Also, increased thoroughness (or extent of skin covered) of the skin self-exam was associated with thinner lesions (Pollitt et al., 2009), and patients who examined at least some parts of their body had thinner lesions at diagnosis compared to those who did not examine their skin (Carli, De Giorgi, Betti, et al., 2003; Pollitt et al., 2009). A case control study (423 melanoma patients and 678 matched controls) found that individuals who conducted SSE were twice as likely to self-detect melanoma and less likely to have thick (advanced) tumours at diagnosis compared to those who did not do SSE (Titus et al., 2013). Finally, in a study with 1,062 melanoma patients (stages I - II), among those who experienced a melanoma recurrence (19%), most recurrences were self-detected (55%) and led directly to

seeking early medical advice (Dalal et al., 2008). Self-detection, not physician detection, independently predicted survival in this study.

Even though cutaneous melanomas are readily visible on the skin surface and it is well-known that SSEs are related to better prognosis (Aitken et al., 2006; Geller et al., 2004; Koh, 1992; Robinson, Fisher, & Turrisi, 2002; Terushkin & Halpern, 2009), most melanoma survivors do not perform whole-body skin exams regularly (Berwick, Begg, Fine, Roush, & Barnhill, 1996; Carli, De Giorgi, Palli, et al., 2003; Manne & Lessin, 2006; Mujumdar et al., 2009). Reported SSE rates among melanoma survivors vary by the modality of asking about the exam and timeframe of assessment. For example, a large cohort study conducted in Australia (n=1433 confirmed melanoma cases) found that 57.4 % of participants had performed an SSE in the past 3 years (Olsen et al., 2015). A cross-sectional study found that among 316 melanoma survivors, 28% reported having ever engaged in SSE, 16% reported doing monthly SSE, and 8% reported doing SSE every 2 months (Glenn, Chen, Chang, Lin, & Bastani, 2016). Another cross-sectional study (n=321 melanoma patients) found that 15% of individuals performed skin checks by examining their moles every 1-2 months, 18% checked their skin every 6 months, and 17 % checked their skin once a year (Pollitt et al., 2009). Coups and colleagues (Coups, Manne, Stapleton, Tatum, & Goydos, 2016) found that 72% of 176 melanoma patients had performed SSE during the last 2 months, but only 14% had examined their whole body.

Predictors of SSE

Personal characteristics that have been associated with SSE include a personal or family history of skin cancer, including melanoma (Aitken et al., 2004; Girgis, Campbell, Redman, & Sanson-Fisher, 1991; Glenn et al., 2016; Robinson et al., 2002), being female, and having a higher level of education (Carli, De Giorgi, Palli, et al., 2003; Glenn et al., 2016; Manne & Lessin, 2006; Olsen et al., 2015; Robinson et al., 2002). Unlike medical and demographic factors linked to SSE, which are not generally amenable to intervention, psychosocial and educational factors associated with SSE are potential targets of interventions that aim to improve adherence to SSE instructions. Psychosocial factors associated with SSE behaviours in melanoma survivors and other high-risk individuals include greater knowledge about melanoma and SSE (DiFronzo, Wanek, & Morton, 2001; Friedman,

Rigel, Silverman, Kopf, & Vossaert, 1991; Robinson et al., 2002), higher perceived susceptibility to melanoma (Azzarello, Dessureault, & Jacobsen, 2006; Glenn et al., 2016; Olsen et al., 2015; Robinson et al., 2002), positive attitude towards SSE (Robinson et al., 2002; Robinson, Turrisi, & Stapleton, 2007), confidence in being able to perform an efficacious skin self-exam (Azzarello et al., 2006; Friedman et al., 1991; Robinson et al., 2002; Robinson et al., 2007), and having a physician recommend SSE (Chiu, Won, Malik, & Weinstock, 2006; Manne & Lessin, 2006; Robinson, Rigel, & Amonette, 1998; Robinson et al., 2007). There is also preliminary evidence that the level of anxiety and the psychosocial strain resulting from a melanoma diagnosis affect self-exam practice (Körner, Augustin, & Zschocke, 2011). Furthermore, being informed about SSE by a health care professional has been shown to be associated with SSE performance.

Some of the limitations of the literature exploring predictors of SSE include the lack of a standardized operationalization of SSE (Coroiu et al., In preparation), which directly affects the reported rates of this behaviour; the limited inclusion of psychosocial variables, such as distress, coping strategies and physician support , as only a few studies have addressed these constructs in relation to SSE; and limited duration of follow-up assessments, as research has shown that the performance of health behaviours decreases over longer time periods (DiMatteo, Giordani, Lepper, & Croghan, 2002; Glanz, Lewis, & Rimer, 2008).

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 mortality. While most melanomas are detected by patients, spouses, and other family members, physician-detected cancerous lesions tend to be thinner, representing an earlier disease stage, than self-detected lesions. Self-examination conducted in tandem with the clinical exam appears to be a desirable and more feasible approach to melanoma early detection than clinical exams alone. Despite SSE being an integral part of clinical guidelines for the prevention of melanoma among at-risk groups, many individuals at risk do not practice SSE regularly or thoroughly. Studies, including randomized controlled trials, have shown that rates of SSE can be improved through patient education, but little is known about those who adhere to SSE clinical recommendations versus those who do not. Acquiring knowledge on the strongest predictors of SSE practice will enable researchers and

clinicians to design intervention protocols targeting core issues in melanoma prevention, and, thus, contribute to improved quality of life for patients, decreased need for invasive (but rarely curative) treatments such as chemotherapy, and ideally improved survival.

Research Objectives

The main objective of this study is to identify short- and long-term predictors of SSE after providing best-practice clinical care, which includes medical advice on SSE, and to better understand challenges and opportunities for secondary prevention of melanoma in high-risk individuals. Specific objectives include:

(1) To determine the extent of SSE behaviour, defined as "SSE comprehensive" (extent of body covered by a skin exam) and "optimal SSE" (monthly exam of the whole body) at 3 months (time point 3), 12 months (time point 4) and 24 months (time point 5) after receiving a standardized dermatological education session on SSE during melanoma follow-up care.

(2) To identify individual-level, psychosocial variables (e.g., self-efficacy, perceived physician support) that are independently associated with SSE at 3, 12, and 24 months following a standardized dermatological education session.

Hypotheses

(1) The prevalence of SSE behaviour will be higher at 3 months post education than at 12 and 24 months, respectively, post a standardized dermatological education on SSE.

(2) Biological sex and psychosocial variables (e.g., attitudes about SSE, knowledge about melanoma, intentions to perform SSE, self-efficacy about SSE) will be significantly associated with SSE behaviour at 3, 12 and 24 months post a standardized dermatological education on SSE.

Method

The current study followed the STROBE guidelines for reporting of observational studies (Von Elm et al., 2007). The study received funding from the Fonds de recherche du Quebec-Santé (FRQS) and the Canadian Institutes of Health Research (CIHR). A detailed study protocol is available (Korner et al., 2013). Ethical approval

for this study was granted by the Institutional Review Board of the Faculty of Medicine, McGill University, the McGill University Health Centre, and the Jewish General Hospital.

Study Design

This is on observational study with longitudinal follow-up (5 time points): enrolment (time point 1), administration of a standardized educational session on best practice for self-surveillance of skin (or SSE) in order to identify problematic lesions (time point 2), assessment of barriers and facilitators of SSE (time point 3) and assessment of outcomes, i.e., SSE behaviour (time points 3, 4, and 5.)

Participants and Procedures

Patients diagnosed with melanoma were recruited from Dermatology-Oncology Clinics of two McGill-affiliated hospitals in Montréal, Québec, Canada. Eligibility for the study included a confirmed diagnosis of melanoma, 18 years of age or older, and proficiency (written, verbal) in English of French. Recruitment was conducted from September 2012 to March 2014 and data collection was completed in October 2016. Extensive efforts were made to approach all of the eligible patients during the recruitment period. Recruitment was conducted in person by trained research assistants (RA) who explained the study procedures, assessed eligibility criteria, and obtained written consent. Consenting patients were offered the option to include their partners (spouses) in the educational session delivered at time point 2.

At enrolment (time point 1) participants were given a brief self-report questionnaire including socio-demographic questions (age, education, ethnic background, etc.) and measures assessing preventive behaviours prior to diagnosis and current psychosocial status (e.g., distress symptoms, coping strategies, social support). Medical data (e.g., time since diagnosis, melanoma stage and depth) were collected from the medical charts. At time point 2, approximately 3 to 6 months post enrolment, we administered a 15-minute educational intervention on SSE modelled by best-practice guidelines of care for individuals at increased risk for melanoma. The intervention was described in detail in the published study protocol (Körner et al., 2013). At time point 3, which took place 3 months post the educational session (EDU), we assessed SSE behaviours and psychosocial predictors of SSE previously identified by the empirical literature (e.g., self-efficacy for and attitudes about SSE).

At time points 4 (12 months post EDU) and 5 (24 months post EDU) we assessed again SSE comprehensive and SSE optimal.

Measures: Independent Variables

Socio-demographic and Medical Information. Individual self-reported data on personal characteristics (e.g., age, sex, education, ethnicity, years lived in Canada, marital status, mother tongue) were collected at enrolment. Disease-specific information, such as date of diagnosis, melanoma stage and depth, and previous cancer diagnoses were collected from the patient medical charts and the pathology reports included in the patient's medical records.

Melanoma Knowledge Questionnaire (Coroiu, Moran, Kwakkenbos, Thombs, & Körner, 2018). Melanoma knowledge was assessed using a 6-item self-report measure covering melanoma risk factors and melanoma preventive behaviours (sample item, "Melanoma can develop a) on any skin surface; b) only on parts of the skin exposed to the sun"). The items were ranked on a 3-point scale ("True", "False", and, "I don't know"). For analyses, the neutral choice (I don't know) was collapsed with the "false" answer choice. Total sum scores computed across the 6 items ranged from 0 to 6. Validation analyses conducted in the current sample found that higher melanoma knowledge scores were associated with younger age, more years of education and higher income and that scores were not associated with biological sex, time since diagnosis, melanoma stage or melanoma thickness, SSE behaviour, or physician support of SSE. (Coroiu et al.).

Attitudes about SSE (Moran, Bergeron, Coroiu, & Körner, 2018). Personal attitudes about SSE, including perceived importance, personal gains and barriers to SSE, were captured with a 6-item measure (sample facilitator item: "By doing skin self-exams, I can find moles or growths on my skin that are cancerous or may become cancerous"; sample barrier item, "I feel uncomfortably reminded of melanoma when I examine my skin"). Response options ranged from 0 (strongly disagree) to 3 (strongly agree), and total scores can range from 0 to 18. Three items (barriers) were reverse coded so that higher scores indicate more positive attitudes towards SSE. Positive attitudes towards SSE were found to be associated with intention to perform SSE in the future (Janda et al., 2004) and SSE compliance (Manne & Lessin, 2006).

Self-Efficacy for SSE (Bergeron, Moran, Coroiu, & Körner, 2018). Self-confidence in performing effective SSE was measured using a 5-item self-report questionnaire. Response options ranged from 0 ("strongly disagree") to 3 ("strongly agree"). Item 3 ("There are so many moles and freckles on my body that performing skin self-exams would be difficult") was reverse coded so that higher total scores indicate higher levels of self-efficacy for SSE, with possible total scores ranging from 0 to 15. A previous investigation of the psychometric properties of the scale in data collected at enrolment found that it was reliable (α=0.74) and positively associated with physician support and intentions to perform SSE (Bergeron et al., Submitted).

Intentions to Perform SSE (Manne & Lessin, 2006). Intentions to perform SSE were assessed using 1 item: "How likely are you to self-examine your skin on a regular basis in the coming year?". The item was scored on a 5-point Likert scale ranging from 1 ("very unlikely") to 5 ("very likely"), with higher scores indicating stronger intentions to perform SSE. In a study assessing intentions and adoption of SSE practice in patients with melanoma, higher intention to perform SSE was associated with female gender, physician recommendation of SSE, and patient perception of barriers and benefits of SSE (Manne & Lessin, 2006).

Physician Support of SSE (Coroiu, Moran, Garland, & Körner, 2018). Perceptions about physicians' interest and concern in patients' practice of SSE was assessed using a 9-item self-report scale (sample item, "My physician has recommended that I do skin self-exams"). The items are scored on a 4-point Likert scale ranging from 0 ("not at all true") to 3 ("true"). The total sum score can range from 0 to 27, with higher scores indicating higher physician support for SSE. The total score showed excellent internal consistency at baseline (α=0.96). Physician support for SSE is associated with prior physician CSE and demonstration of SSE by a health care professional (Coroiu et al., 2018).

Patient Health Questionnaire-4 (PHQ-4) (Kroenke, Spitzer, Williams, & Löwe, 2009). The PHQ-4 is a 4-item scale assessing symptoms of depression (sample item, "Little interest or pleasure in doing things") and anxiety (sample item, "Not being able to stop or control worrying") over the past 2 weeks. The items are scored on a three-point scale, ranging from 0 ('not at all') to 3 ('nearly every day'). Total scores can range from 0 to 12, with higher scores indicating higher distress levels. In a sample of patients seeking treatment in primary-care

settings, PHQ-4 scores were strongly associated with functional impairment and higher healthcare usage (Kroenke et al., 2009). Higher PHQ-4 scores were also associated with longer duration of hospital stay, higher likelihood of re-hospitalization within 90 days and of death in patients with advanced cancer (Nipp et al., 2017).

Skin Cancer Index (SCI) (Rhee et al., 2006). Disease-specific emotional, social and appearance-related distress were assessed using a 15-item measure. This self-administered questionnaire asks about skin cancer worries in the past month (sample item, 'During the past month, how much have you… felt anxious about your skin cancer'). Response options range from 1 ('very much') to 5 ('not at all'), for a total possible sum score of 15 – 75. Items were reverse coded to improve comparability to other measures in the current study, where higher scores indicate higher levels of the measured construct. This scale demonstrated a high level of internal consistency ($0.82>\alpha>0.92$) and good convergent and divergent validity among skin cancer patients (Rhee et al., 2006), and is sensitive to detect changes in distress post-surgical treatment (Rhee et al., 2007).

Reliance on Medical Advice (FKV-2). The two-item subscale "compliance/ trust in doctor" of the Freiburg Questionnaire of Coping with Illness (FKV) [Freiburger Fragebogen zur Krankheitsverarbeitung] (Muthny, 1989) was used to assess coping with melanoma by relying on medical advice ("I follow the medical advice exactly" and "I trust my doctors"). Response options ranged from 1 ('not at all') to 4 ('very much') with possible total scores between 2 and 8. Higher scores indicate more use of coping by adhering to medical advice. Items from this German scale were translated to English using forward-backward translation procedure (Acquadro et al., 2008; Cha, Kim, & Erlen, 2007). The total FKV scale (35 items) has shown good psychometric properties in a variety of samples with chronic illnesses (Muthny, 1989) and the here used subscale had an acceptable internal consistency of 0.69 in a cancer sample (Hardt et al., 2003).

Constructive Attitudes towards Health. The 5-items constructive attitudes subscale of the Health Education Impact Questionnaire (heiQ) (Osborne, Elsworth, & Whitfield, 2007) was used to assess constructive attitudes and approaches to managing challenges of the cancer experience (sample item, "I try not to let my health problems stop me from enjoying life"). Response options range from 0 ('strongly disagree') to 3 ('strongly agree'), with possible total scores between 0 and 15 and higher scores indicating increased attempts

to minimize detrimental effects of illness upon one's life. The heiQ questionnaire was originally developed to evaluate patient self-management and education programs (Osborne et al., 2007). Its adaptation to the cancer context was found to be reliable and valid in a large sample of Canadian cancer survivors, where sum scores of the constructive attitudes and approaches subscale were associated with self-efficacy and productive communication, and improved emotional and mental health (Maunsell et al., 2014).

Measures: Dependent Variables

SSE Behaviour. There is no commonly accepted way to assess SSE behaviour in the melanoma prevention literature (Coroiu et al., In preparation). The items used to assess SSE in this study were developed based on consultation with other melanoma prevention research teams and using materials from published literature. SSE behaviour was assessed using 7 items, which inquired about the frequency of examination of the skin for problematic lesions during the previous 3 months (e.g., "In the last 3 months, how often did you examine …"). We intended to evaluate whether the skin exam covered the entire body, so we divided the body into 5 separate body parts, each corresponding to one item: 1) head and neck (face, neck and scalp), 2) front upper body (stomach, check, arms and shoulders), 3) front lower body (legs, genital/hip areas, top and bottom of feet, between toes), 4) back upper body (upper and lower back), 5) back lower body (buttocks and back of legs). Two additional items were created to evaluate whether participants had correctly examined the back areas, as those necessarily require using mirrors or someone else to assist with the exam ("In the last three months, how often did you have someone else help you with the skin self-exam" and "In the last three months, how often did you use a mirror for skin self-exams). Responses were scored on a 6-point scale: 0 ('never'), 1 ('once every 3 months'), 2 ('once every 2 months'), 3 ('once a month'), 4 ('once a week'), 5 ('more often'). To score the SSE behaviour variables, we collapsed answer choices 4 ('once a week') and 5 ('more often') into one answer, as there is no evidence to suggest a benefit of weekly or more frequent SSE compared to monthly SSE. Further, we compared participants' answers to the items asking about the exam of the back areas (items 3, 4, 5) against the answers to the items inquiring about help with the skin exams, using mirrors or another person (items 6, 7), and adjusted the responses to the respective body parts to match the highest answer on one of the

help items. Our rationale for scoring the SSE behaviour variable in this manner was that participants could not correctly check the lower back, for example, unless they also used mirrors or were assisted by someone.

SSE Comprehensive. Our operationalization of SSE comprehensive was the *frequency of examining 5 body parts in the last three months*. We computed a sum score across the 5 body part items, using corrected scores for the items asking about the back areas, as per scoring methodology described above. Possible scores ranged from 0 to 20, where higher scores indicated more comprehensive skin self-exams.

SSE Optimal. This variable was operationalized as (at least) monthly self-exam *of the complete body, i.e., all five body parts, over the last 3 months*. To compute this variable, we used the 5 body part items with corrected scores for the items asking about the back areas, as per scoring methodology described above, which we dichotomized into 1= if it was reported that all of the 5 body parts were checked at least monthly ("monthly" or "more often") or 0 = if it was reported that any of the 5 body parts were checked less often than monthly ("once every 3 months" or "once every 3 months").

Data Analysis Plan

Power analysis. Power analysis was computed for the continuously measured outcome, i.e., SSE comprehensive. With a projected sample size of N=200, a minimal R^2 increment of .08 was to be detected with .79 power. The power for detecting a R^2 increment of .09 would have been .85. We anticipated a 30-40% attrition, as per previous reports of studies with the similar populations and study duration. Depending on the actual attrition and missing data rates, sensitivity analyses were going to be performed.

Objective 1. Descriptive statistics (means, standard deviations, percentages) will be computed for all of the variables included in the study: predictor variables were assessed at enrolment (socio-demographic variables) and at time point 3 (psychosocial variables); dependent variables (SSE comprehensive and SSE optimal) were assessed at time points 3, 4, and 5. Changes in the outcomes from time 3 to time 4 and time 3 to time 5 will be assessed using Generalized Estimating Equations (GEE) (Hardin & Hilbe, 2002; Liang & Zeger, 1986). GEE has advantages over the traditional repeated measures (e.g., ANOVA): it increases power by increasing degrees of freedom; it increases power by accounting for the dependency of observations by using

a covariate structure of the repeated measurements (whereas ANOVA assumes equal correlation between observations over time); it is robust in managing missing data (e.g., for studies using more than 2 follow-ups, the GEE analysis retains pairs of data at two time points, whereas ANOVA would exclude any cases without 3 data points); it can be used with non-normally distributed data; and it can be used with continuous and categorical predictors and outcomes (whereas ANOVA assumes categorical predictors) (Lim et al., 2017). Finally, GEE was chosen over mixed effects models because our objective was to calculate average population prognosis in order to draw population-based conclusions to inform policy and health decisions as opposed to examining changes at the individual level, such as the trajectory of change in scores of one particular participant (Lim et al., 2017). We estimated the changes in the outcomes over time using the Generalized Linear Models and GEE functions in SPSS v.23 and fit a linear model for the continuous outcome, SSE comprehensive, and a binary logistic model (binomial distribution) for the dichotomous outcome, SSE optimal. We pre-imposed an auto-regressive correlation structure to the data, which is consistent with our a priori hypothesis that SSE behaviour will decrease over time.

Objective 2.1: Predictors of SSE Comprehensive. Three hierarchical multiple regressions will be performed to predict SSE comprehensive at 3 months post EDU (time point 3), 12 months post EDU (time point 4) and 24 months post EDU (time point 5). The predictors will be entered in blocks as follows: 1) gender, 2) melanoma knowledge, attitudes about SSE, and intentions about SSE, 3) self-efficacy about SSE, 4) skin cancer index and the PHQ-4, 5) constructive attitudes and approaches subscale of the heiQ subscale and FKV-2. The blocks were chosen based on a) previous literature which reported gender differences in the practice of SSE; b) the information-motivation-behavioural skills model of behavioural change which posits that individuals who are knowledgeable (informed about personal risk and preventive strategies that can mitigate risk), motivated (e.g., positive attitudes towards the health behaviour; increased intentions to perform the behaviour) and feel self-efficacious about performing a preventive health behaviour are more likely to adhere to and maintain engagement in such behaviour over time (Fisher & Fisher, 1992, 2002); and c) our team's preliminary work and

clinically-informed expectations that distress and coping strategies might play a role in the adoption and maintenance of SSE behaviours .

Objective 2.2: Predictors of SSE Optimal. Bivariate logistic regressions will be performed with socio-demographic, medical and psychosocial variables as predictors and SSE optimal at 3, 12, and 24 months post EDU as dependent variables. Multivariate logistic regressions (adjusted for all predictors) will also be conducted.

Results

Study Characteristics

A total of 477 potentially eligible individuals were approached in person about participating in this study, of which 188 declined participation and 289 gave informed consent (response rate 61%). Of those who gave consent, eight individuals did not meet eligibility criteria (either were diagnosed with a skin cancer other than melanoma or had participated in our pilot study) and 39 did not return the baseline questionnaire. A total of 242 melanoma patients were enrolled in the study and completed socio-demographic questionnaires at time points 1; 189 completed the educational session offered at time point 2 (3-6 months after enrolment); 165 completed the first follow-up assessment administered at time point 3 (3 months post the educational session), 160 completed the second assessment administered at time point 4 (12 months after the educational session), and 124 completed the third and last assessment (time point 5; 24 months post the educational session). The recruitment and participation flowchart is included in Figure 1. The attrition rate was 32% at the first follow-up, 34% at the second follow-up, and 49% at the third follow-up. In this report we included participants who completed at least the first follow-up appointment (n=165). Table 1 includes sample characteristics: descriptive statistics for the socio-demographic and medical variables and all of the study measures. Half of our sample were females, the mean age was 60, the average number of years of education was 15 and about half of the sample had been diagnosed with stage I melanoma.

Objective 1: Prevalence of SSE behaviour and changes over time

SSE Comprehensive. The mean score for SSE comprehensive (defined as the frequency of checking the 5 body parts, corrected for the help of a mirror or another person to check the back of the body; assessed on a scale of 0 to 20) decreased over time from 13.2 at the 3 months follow-up, to 12.5 at 12 months post, and 11.8 at 24 months post, as shown in Table 1. Statistically significant differences were observed between the means reported at 24 months versus 3 months post education session, as shown in Table 2. There were no statistical differences between the scores reported at 12 months versus 3 months post education.

SSE Optimal. The percentage of individuals who performed optimal SSE (defined as monthly checking of all 5 body parts including the use of a mirror or another person to check the back of the body) decreased over time, from 57% at 3 months post, to 44% at 12 months post, and 36% at 24 months post, as shown in Table 1. Statistically significant decreases in the proportion of SSE optimal were observed from 3 months to 12 months ($p=.004$) post and from 3 months to 24 months ($p < .001$) post, as shown in Table 3.

Objective 2.1: Predictors of SSE Comprehensive

In hierarchical multiple regressions the significant predictors of SSE comprehensive at 3 months follow-up were biological sex, SSE intentions, FKV-2, and constructive attitudes and approaches (heiQ). Specifically, male gender, higher intentions to perform SSE, increased reliance on medical advice (FKV-2) and lower constructive attitudes (heiQ) were associated with increased SSE comprehensiveness. Melanoma knowledge, SSE attitudes, SSE self-efficacy, SCI, and PhQ4 were not significant predictors of SSE. The final model explained 37% of the variance in the SSE comprehensive scores.

The significant predictors of SSE comprehensive at 12 months follow-up were SSE attitudes and SSE intentions. Specifically, more positive attitudes towards SSE and higher intentions to perform SSE were associated with increased SSE comprehensiveness. No other variables were significant predictors. The final model explained 28% of the variance in the SSE comprehensive scores.

The only significant predictor of SSE comprehensive at 24 months follow-up were SSE intentions, where higher intentions to perform SSE were associated with increased SSE comprehensive. The final model explained 27% of the variance in the SSE comprehensive scores.

Objective 2.2: Predictors of SSE Optimal

In bivariate logistic regressions, variables significantly associated with an increased likelihood of SSE at 3 months follow-up included SSE attitudes, SSE intentions, SSE self-efficacy, reliance on medical advice (FKV-2), constructive attitudes and approaches (heiQ), and physician support of SSE. In multivariate logistic regressions (with all covariates entered in one step), SSE intentions and SSE self-efficacy were the strongest predictors of SSE optimal at 3 months follow-up.

In bivariate logistic regressions, variables significantly associated with an increased likelihood of optimal SSE at 12 months follow-up included SSE attitudes, SSE intentions, SSE self-efficacy, and FKV-2. In multivariate logistic regressions, none of the predictors were significantly associated with optimal SSE at the 12 months follow-up.

In bivariate logistic regressions, variables significantly associated with an increased likelihood of SSE at 24 months follow-up included SSE attitudes, SSE intentions, SSE self-efficacy, skin cancer specific distress (SCI), and physician support of SSE. In multivariate logistic regressions, SSE self-efficacy and distress (SCI) were the strongest predictors of SSE optimal at the 24 months follow-up.

Discussion

The main objectives of this observational study with longitudinal follow-up was to assess the prevalence of SSE behaviours over time, conceptualized as SSE comprehensive and SSE optimal performance, and to assess the predictors of these two outcomes at 3, 12, and 24 months after a standardized educational session. SSE comprehensive was conceptualized as frequency and extent of skin covered during the skin exam while accounting for help with checking the back of one's body. SSE optimal was conceptualized as monthly, complete (entire body) skin exam while again accounting for help in order to check the back. The standardized educational session was designed to match the prevention strategies (information on early signs of melanoma

and demonstration of how to perform SSE) recommended by dermatology associations and clinical care guidelines for patients in melanoma follow-up care. As hypothesized, we found that both SSE behaviours, SSE comprehensive and SSE optimal, where higher at 3 most follow-up than at subsequent follow-ups and decreased significantly by 24 months post the educational session.

Our second hypothesis was only partially supported. Biological sex was associated with SSE comprehensiveness only at the 3 months follow-up with males reporting more comprehensive SSE than females. Intentions to perform SSE predicted the comprehensiveness of the skin exam consistently at all three follow-ups. Our analyses were guided by the information-motivation-behavioural skills model which posits that individuals, who are well informed and motivated to perform or to adopt health behaviours, are likely to develop self-efficacy skills which in turn lead them to adopt and maintain the health behaviour (Fisher & Fisher, 1992, 2002). We did not find support for this model when we tested predictors of SSE comprehensive, as melanoma knowledge, attitudes about SSE, and self-efficacy about SSE did not predict SSE. Distress did not predict comprehensiveness of SSE at any of the follow-ups. Coping strategies were related to the comprehensiveness of SSE only at the 3 months follow-up, but not at later assessment points. It appears that higher intentions to perform a skin exam is the single, most important predictor of a thorough, whole-body SSE, in the short-term and long-term. The strongest predictors of adherence to monthly, whole-body SSE recommendations (i.e., SSE optimal) included SSE intentions and confidence in one's ability to perform an efficacious skin exam (i.e., SSE self-efficacy) at 3 months post education, and SSE self-efficacy and skin cancer specific distress at 24 months post education. At the 12 months follow-up, no significant predictors of SSE optimal were identified in analyses adjusted for all predictors.

The reported rates of SSE behaviour found in this study are higher than those previously reported in cross-sectional studies (Olsen et al, 2015 2015, Glenn et al, 2016, Pollitt et al, 2009). This is most likely due to the fact that we offered all of our participants a standardized educational session on how to adequately examine one's skin to identify problematic lesions, which increased SSE-related self-efficacy (Czajkowska, Hall, Sewitch, Wang, & Körner, 2017) and raised awareness of the risk for developing subsequent melanomas. To our

knowledge, this is the first study in the literature to follow participants in melanoma follow-up care for as long as 24 month and periodically assess their self-surveillance (skin checking) behaviours in order to identify the key predictors of this behaviour under the condition of best-practice in the context of secondary prevention of melanoma.

Limitations

There are some limitations of this study, which primarily relate to our sampling procedures, the study design, and the measurement of the behavioural outcomes. First, we aimed to include as many eligible participants as were seen at our recruitment's centers during the active phase of the study. However, the skin cancer clinics were extremely busy, and some patients stayed on the premises strictly for the medical check-up which made it difficult for us to approach them. It is possible that we missed some participants who would have been eligible and could have provided valuable data to the study. Second, this is an observational study with longitudinal design, so we anticipated a 30% level of attrition. However, as the study extended to 24 months post the educational session, that is at least 27 months post enrolment, we experienced higher than expected loss to follow-up. For the current analyses we did not do imputations and chose to reported results from study completers, which reduces our sample size considerably over time. Smaller numbers at subsequent time points affect the precision of the estimates reported and might affect the generalizability of our findings to other populations. Also, it is also possible that SSE behaviours were lower among individuals who did not complete the study. Last, this study assessed the main outcomes via self-report measures for which there is no evidence supporting their validity or reliability, and no standardized method of assessing SSE currently exists. While we created the items based on items used in previous studies and extensive literature searches and consultation with experts, this might nonetheless affect the validity of our findings.

Implications and Directions for Future Research

As this study shows that rates of SSE decrease over time, future intervention studies with longer follow-up should include reminders, or booster sessions, as melanoma patients continue to experience increased risk even 20 years past their diagnosis. Also, future studies might consider including in the intervention specific

instructions about seeking a medical opinion when problematic lesions are detected and to assess whether people adhere to such recommendations. The current study found that the single most consistent predictor of SSE was people's intentions to perform the behaviour. An explanation for it is that we used a high-risk sample in active follow-up by a dermatologist, so our participants may have had increased motivation to perform preventive behaviours. It is also possible that our educational session boosted people's motivation through the reinforcement of the benefits of such behaviour for the early detection of melanoma. Further, at our recruiting hospitals, dermatologists routinely recommended lifelong SSE to all of their melanoma patients. Other samples might benefit from brief Motivational interviewing sessions addressing barriers to change and to the adoption of screening behaviours. Future studies should necessarily address the questions whether SSE facilitates early detection and whether early detection via SSE and a timely clinical exam can reduce mortality. Melanoma cohort studies might be the most feasible approach for providing answers to such questions. Unfortunately, in Canada, there is no melanoma registry or a cohort, which could assist in finding answers to questions about secondary prevention and the early detection of this deadly disease.

Conclusion

To our knowledge, this is the first study in the literature addressing the short (3 months) and long-term (12 and 24 months) predictors of SSE behaviour in a sample of melanoma patients receiving ongoing follow-up care. As anticipated, we found that SSE behaviour is more frequent and comprehensive and also more likely to be conducted as per recommended guidelines in the short-term compared to later after being educated about skin self-examination. In the short and long-term, intentions to perform SSE predicted SSE comprehensive (extent of body covered by the skin exam) and self-efficacy for SSE predicted adherence to optimal SSE (monthly checking of entire body). These results have implications for the design of future melanoma prevention interventions, as intentions for SSE and self-efficacy for SSE are highly amenable to change and can be targeted by psycho-social intervention with at-risk people.

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Conflict of Interest:

The authors declare that there is no conflict of interest.

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Table 1. Characteristics of the Study Sample

Variable Name	Q1 (1st quartile)	Q2 (median)	Q3 (3rd quartile)	Mean (SD)	N (%)
Sex (F)					122 (50.6)
Age (in years)	50	60	69	59.5 (13.8)	
Education (in years)	12	15	17	14.8 (3.5)	
Melanoma Stage					
0 (In situ)					39 (16.4)
1					119 (50.0)
2					55 (23.1)
3					17 (7.1)
4					8 (3.4)
Time since diagnosis (in weeks)	6	30.5	155	121.7 (220.3)	
SSE self-efficacy	9	10	12	10.0 (2.5)	
SSE intentions	4	5	5	4.4 (0.9)	
SSE physician support	12	21	25	17.7 (8.9)	
SSE attitudes	10	12	14	11.8 (2.6)	
SCI	21	27	36	29.9 (11.8)	
PHQ-4	0	0	3	2.1 (3.2)	
Reliance on medical advice (FKV-2)	7	8	8	7.3 (1.0)	
Constructive attitudes (heiQ)	10	11	15	7.3 (1.0)	
SSE optimal					
3-month FU					94 (57.0)
12-month FU					70 (43.8)
24-month FU					44 (35.5)
SSE comprehensive					
3-month FU	10	15	16	13.2 (5.0)	
12-month FU	9	14	17	12.5 (5.4)	
24-month FU	7	12	16	11.8 (5.5)	

Note. SSE = skin self-examination; SCI = Skin Cancer Index; PHQ-4 = Patient Health Questionnaire-4; FKV-2 = 2 items of the Freiburg Questionnaire of Coping with Illness; Constructive attitudes and approaches subscale of heiQ = The Health Education Impact Questionnaire; FU = follow-up; EDU=standardized educational session. Age, education assessed at enrolment. Melanoma stage at diagnosis collected from the patient medical charts.

Time since diagnosis computed using the date of diagnosis extracted from the medical charts and the date of enrolment. SSE self-efficacy, SSE intentions, SSE attitudes, SCI, PHQ-4, FKV, and heiQ assessed at 3 months post EDU. SSE behaviour was assessed at 3, 12, and 24 months post EDU.

Table 2. GEE Parameter Estimates for Longitudinal Changes in SSE Comprehensive

Variable	b (SE)	95% CI	Wald (df)	p
Main effect of time				
SSE Comprehensive: 3-month FU	REF	REF	REF	REF
SSE Comprehensive: 12-month FU	-0.74 (0.43)	-1.57, 0.10	2.98 (1)	.084
SSE Comprehensive: 24-month FU	-10.91 (0.36)	-11.62, -10.21	924.0 (1)	<.001

Note. GEE = generalized estimating equations; SSE = skin self-examination; FU = follow-up; EDU = standardized educational session.
Sample of patients included by time point: FU1=164, FU 2=157, FU 3=119.

Table 3. GEE Parameter Estimates for Longitudinal Changes in SSE Optimal

Variable	OR	95% CI	Wald (df)	p
Main effect of time				
SSE optimal: 3-month FU	REF	REF	REF	REF
SSE optimal: 12-month FU	0.60	0.42, 0.85	8.44 (1)	.004
SSE optimal: 24-month FU	0.40	0.27, 0.60	19.40 (1)	<.001

Note. GEE= generalized estimating equations; OR = odds ratio; SSE = skin self-examination; FU = follow-up; EDU = standardized educational session.
Sample of patients included by time point: FU1 =165, FU2 =160, FU3 =124.

Table 4. Hierarchical Linear Regression Models Predicting SSE Comprehensive

Variable	3-month follow-up (n=151)				12-month follow-up (n=134)				24-month follow-up (n=105)			
	R^2	ΔR^2	ΔF	β	R^2	ΔR^2	ΔF	β	R^2	ΔR^2	ΔF	β
Model 1	.01	.01	2.08		.001	.001	.07		.005	.005	0.47	
Sex				-0.12				-.02				0.07
Model 2	.31	.30	21.23*		.23	.23	13.12*		.24	.24	10.49*	
Sex				-0.21**				-0.12				-0.03
Melanoma knowledge				0.04				0.01				0.01
SSE attitudes				0.08				0.19**				0.19
SSE intentions				0.53*				0.42*				0.41*
Model 3	.33	.01	2.63		.25	.02	3.31		.26	.06	2.56	
Sex				-0.22**				-0.11				-0.05
Melanoma knowledge				0.06				-0.02				0.03
SSE attitudes				0.08				0.17				0.20
SSE intentions				0.53*				0.34**				0.39*
SSE self-efficacy				0.11				0.16				0.14
Model 4	.33	.001	0.41		.28	.03	2.26		.27	.01	0.82	
Sex				-0.22**				-0.10				-0.05
Melanoma knowledge				0.06				-0.04				0.02
SSE attitudes				0.06				0.20**				0.22
SSE intentions				0.52*				0.29**				0.36*
SSE self-efficacy				0.11				0.17				0.14
SCI				0.07				0.10				0.08
PHQ-4				-0.02				-0.19				-0.13

Variable	3-month follow-up (n=151)				12-month follow-up (n=134)				24-month follow-up (n=105)			
	R^2	ΔR^2	ΔF	β	R^2	ΔR^2	ΔF	β	R^2	ΔR^2	ΔF	β
Model 5	.37	.04	4.43**		.28	.00	0.03		.27	.00	.00	
Sex				-0.19**				-0.10				-0.05
Melanoma knowledge				0.07				-0.04				0.02
SSE attitudes				0.03				0.19**				0.22
SSE intentions				0.52*				0.55**				0.36*
SSE self-efficacy				0.09				.018				0.14
SCI				0.06				0.10				0.08
PHQ-4				-0.09				-0.19				-0.13
Reliance on medical advice (FKV-2)				0.15**				0.01				0.00
Constructive attitudes (heiQ)				-0.19**				-0.02				-0.01
	Overall F (9, 141) = 9.16, p < .001				Overall F (9, 124) = 5.35, p < .001				Overall F (9, 95) = 3.99, p < .001			

Note. SSE = skin self-examination; SCI = Skin Cancer Index; PHQ-4 = Patient Health Questionnaire-4; FKV-2= two items of the Freiburg Questionnaire of Coping with Illness; Constructive attitudes and approaches subscale of heiQ = The Health Education Impact Questionnaire;
*p < .001, **p <.05

Table 5. Logistic Regressions Predicting SSE Optimal

Variable Name	3-month follow-up				12-month follow-up				24-month follow-up			
	SSE optimal (n=94)	SSE not optimal (n=71)	Crude OR [95% CI]	Adj* OR [95% CI] (n=126)	SSE optimal (n=70)	SSE not optimal (n=90)	Crude OR [95% CI]	Adj * OR [95% CI] (n=113)	SSE optimal (n=44)	SSE not optimal (n=80)	Crude OR [95% CI]	Adj* OR [95% CI] (n=92)
Sex, Female	43 (45.7)	42 (59.2)	0.58 [0.31, 1.09]	0.24 [0.07, 0.81]	34 (48.6)	47 (52.2)	0.86 [0.46, 1.61]	1.17 [0.44, 3.08]	19 (43.2)	38 (47.5)	1.19 [0.57, 2.50]	1.24 [0.28, 5.42]
Age	59.3 ± 12.6	59.0 ± 13.9	1.00 [0.98, 1.03]	0.97 [0.93, 1.02]	59.6 ± 11.9	59.2 ± 15.3	1.0 [0.98,1.03]	1.00 [0.96,1.04]	57.8 ± 12.8	60.6 ± 13.6	0.98 [0.96, 1.01]	0.94 [0.88, 1.01]
Education, in years	14.6 ± 3.4	15.2 ± 3.3	0.95 [0.86, 1.04]	0.96 [0.81, 1.14]	14.1 ± 3.2	15.3 ± 3.3	0.90 [0.81, 0.99]	0.86 [0.73, 1.02]	13.3 ± 2.8	15.8 ± 3.3	0.77 [0.67, 0.89]	**0.75 [0.59, 0.96]**
Stage 0 (in situ)	13 (13.8)	14 (20.6)	REF	REF	7 (10.0)	18 (20.5)	REF	REF	3 (6.8)	17 (22.1)	REF	REF
1	47 (50)	37 (54.4)	1.37 [0.57, 3.26]	0.50 [0.10, 2.47]	31 (44.3)	50 (56.8)	1.60 [0.60, 4.25]	0.61 [0.15, 2.49]	22 (50.0)	41 (53.3)	3.04 [0.80, 11.52]	NE
2	22 (23.4)	14 (20.6)	1.69 [0.62, 4.64]	0.61 [0.10, 3.87]	22 (31.4)	16 (18.2)	3.54 [1.12, 10.46]	2.21 [0.44, 10.99]	14 (31.8)	15 (19.5)	5.29 [1.27, 22.04]	NE
3	7 (7.5)	3 (4.4)	2.51 [0.53, 11.83]	0.58 [0.05, 6.98]	5 (7.1)	4 (4.6)	3.21 [0.66, 15.58]	1.10 [0.09, 13.06]	3 (6.8)	4 (5.2)	1.25 [0.61, 29.45]	NE
4	5 (5.3)	0 (0.0)	NE	NE	5 (7.1)	0 (0)	NE	NE	2 (4.6)	0 (0)	NE	NE
Time since diagnosis (in weeks)	121.8 ± 237.9	114.4 ± 161.1	1.00 [0.99, 1.00]	1.00 [1.00, 1.01]	119.0 ± 206.6	121.2 ± 214.0	1.00 [0.99, 1.00]	1.00 [1.00, 1.01]	95.3 ± 183.9	127.5 ± 219.5	1.00 [0.99, 1.01]	1.00 [0.99, 1.01]
Melanoma knowledge	4.9 ± 1.3	5.0 ± 1.3	0.94 [0.74, 1.21]	0.86 [0.54, 1.37]	5.0 ± 1.1	5.0 ± 1.4	1.00 [0.77, 1.30]	1.17 [0.79, 1.73]	4.9 ± 1.0	4.9 ± 1.4	1.00 [0.74, 1.35]	0.98 [0.48, 1.99]
SSE attitudes	11.9 ± 2.4	11.5 ± 2.9	1.06 [0.94, 1.20]	0.89 [0.70, 1.12]	12.5 ± 2.6	11.5 ± 2.6	**1.16 [1.01, 1.32]**	1.03 [0.82, 1.29]	12.6 ± 2.2	11.5 ± 2.6	**1.21 [1.03, 1.42]**	0.97 [0.66, 1.42]

Variable Name	3-month follow-up				12-month follow-up				24-month follow-up			
	SSE optimal (n=94)	SSE not optimal (n=71)	Crude OR [95% CI]	Adj* OR [95% CI] (n=126)	SSE optimal (n=70)	SSE not optimal (n=90)	Crude OR [95% CI]	Adj * OR [95% CI] (n=113)	SSE optimal (n=44)	SSE not optimal (n=80)	Crude OR [95% CI]	Adj* OR [95% CI] (n=92)
SSE intentions	4.8 ± 0.6	3.9 ± 1.0	**5.31 [2.94, 9.59]**	**5.20 [2.25, 11.98]**	4.7 ± 0.6	4.2 ± 1.0	**2.47 [1.47, 4.14]**	1.78 [0.91, 3.47]	4.8 ± 0.4	4.3 ± 1.0	**3.50 [1.61, 7.60]**	4.64 [0.91, 23.56]
SSE self-efficacy	10.9 ± 2.0	8.8 ± 2.6	**1.57 [1.31, 1.89]**	**1.44 [1.10, 1.90]**	10.9 ± 2.3	9.4 ± 2.6	**1.29 [1.11, 1.50]**	1.15 [0.93, 1.42]	11.2 ± 2.1	9.5 ± 2.5	**1.35 [1.13, 1.63]**	**1.40 [1.02, 1.94]**
SCI	29.5 ± 11.4	29.6 ± 11.5	1.00 [0.97, 1.03]	0.99 [0.95, 1.05]	32.3 ± 12.3	29.1 ± 12.0	1.02 [0.99,1.05]	1.03 [0.98, 1.09]	33.5 ± 13.1	28.0 ± 11.1	**1.04 [1.00, 1.07]**	**1.06 [0.99, 1.15]**
PHQ4	2.1 ± 3.1	2.3 ± 3.4	0.98 [0.89, 1.08]	1.05 [0.84, 1.32]	1.8 ± 2.6	2.4 ± 3.6	0.93 [0.84, 1.04]	0.93 [0.75, 1.14]	2.0 ± 2.8	2.1 ± 3.5	1.00 [0.88, 1.11]	0.75 [0.51, 1.11]
FKV-2	7.4 ± 1.0	7.1 ± 0.9	**1.56 [1.09, 2.24]**	1.77 [0.93, 3.39]	7.4 ± 1.2	7.0 ± 0.8	**1.43 [1.00, 2.05]**	1.74 [0.98, 3.09]	7.4 ± 1.0	7.2 ± 0.9	1.36 [0.86, 2.16]	1.20 [0.57, 2.52]
heiQ	11.5 ± 2.9	11.8 ± 3.2	0.96 [0.87, 1.07]	0.85 [0.67, 1.07]	11.6 ± 2.8	11.6 ± 3.2	1.00 [0.90, 1.11]	0.91 [0.75, 1.11]	11.6 ± 3.0	12.0 ± 3.1	0.96 [0.85, 1.09]	0.89 [0.68, 1.16]
SSE physician support	18.9 ± 8.5	16.0 ± 9.8	**1.04 [1.00, 1.08]**	-	17.2 ± 8.9	16.9 ± 9.6	1.00 [0.96, 1.05]	-	20.9 ± 7.9	15.5 ± 10.2	**1.07 [1.00, 1.13]**	-

Note. Statistics for the SSE endorsed/not endorsed were presented as n (%) or M ± SD, where M = mean and SD = standard deviation; NE = Not estimable.
SSE= Skin self-examination; CSE = clinical skin examination; SCI = Skin Cancer Index; PHQ-4 = Patient health Questionnaire-4; two items of the Freiburg Questionnaire of Coping with Illness; Constructive attitudes and approaches subscale of heiQ = The Health Education Impact Questionnaire;
*Adjusted for all of the study measures, except for SSE physician support, due to low n.

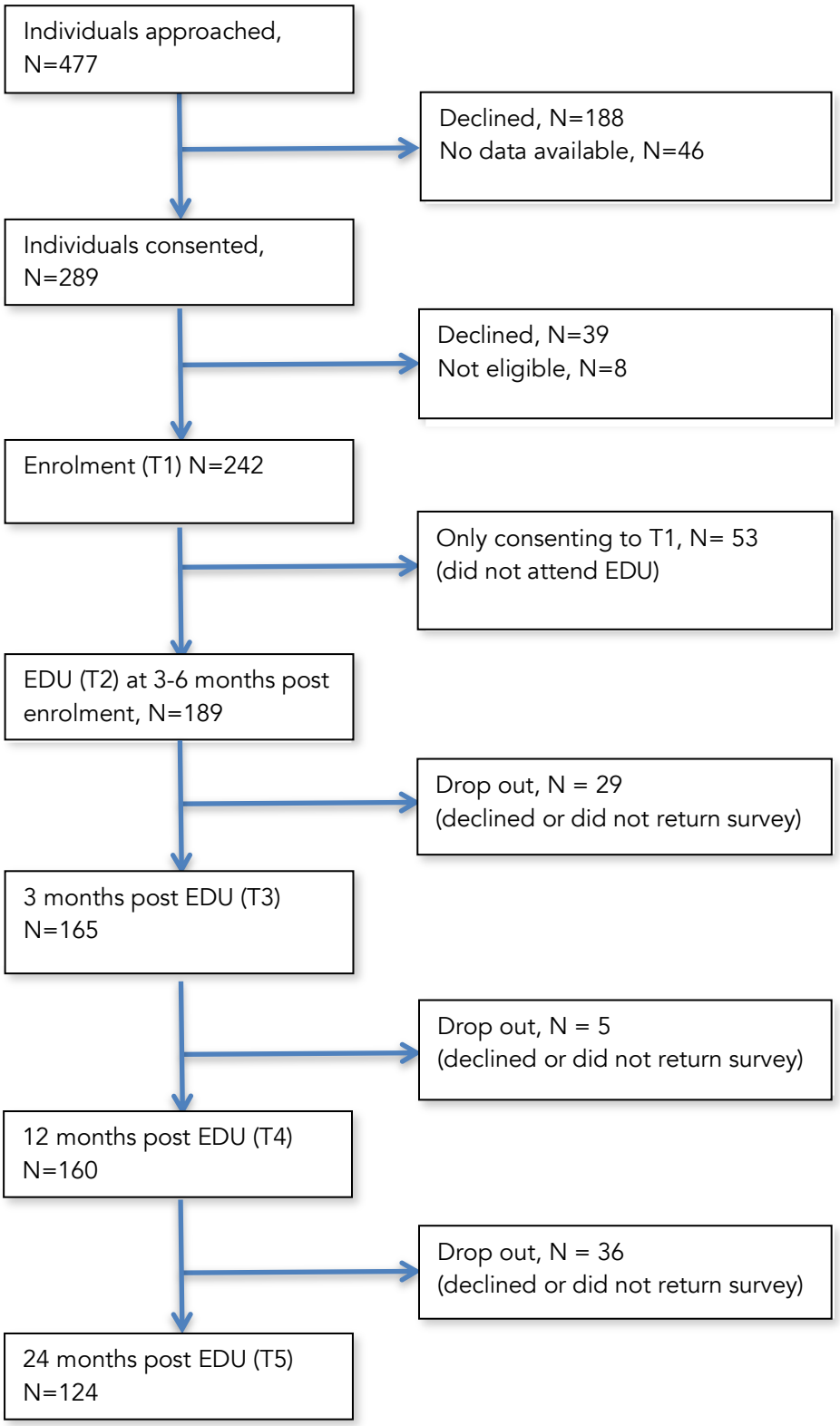

Figure 1. Participation flowchart.
Note. EDU – standardized educational session

General Discussion

The objective of this dissertation was to provide a comprehensive picture of how skin self-examination (or SSE) is typically defined in the melanoma prevention literature and also about the factors that contribute or impede the uptake of this melanoma prevention behaviour among individuals at an increased risk for melanoma. Three separate manuscripts included in this thesis address various aspects about SSE, such as the operationalization of SSE behaviour, the effect of interventions that promote SSE, and the short- and long-term predictors of SSE among at-risk individuals. The overall goal was to inform public health policy about efficient modalities to promote SSE among high-risk groups.

Summary of Main Findings, Limitations and Directions for Future Research

The objectives of the first manuscript were to investigate a) how SSE was defined (conceptualized); b) how SSE was assessed; c) the consistency of methods used to assess SEE; and d) the evidence supporting the validity and reliability of SSE measures used in randomized controlled trials (RCT) of behavioural interventions with individuals at an increased risk for melanoma. This systematic review identified 12 relevant RCT. All of the trials provided recommendations that participants perform SSE, but only 5 trials reported the specific details as to what the recommended SSE behaviours entailed, e.g., periodic checking of the skin on the entire body to identify potentially cancerous lesions using the ABCDE criteria (asymmetry, border, color, diameter, and evolution). In terms of SSE assessment, the number of items used to measure SSE behaviour ranged from 1 (generic item inquiring about skin exams) to 17 (each item inquiring about the skin exam of a different body part); items were scored as either continuous or dichotomous; timeframe of assessment ranged from "last two months" to "last 12 months". Overall, four different modalities of assessing SSE, depending on how the items were phrased, were identified. More specifically, the SSE items inquired about a) whether SSE was performed individually, with a partner, or with tracking or monitoring devices; b) the comprehensiveness (completeness) of SSE relative to the extent of the skin checked (i.e., few body parts, many body parts, entire body, or all moles; c) the recency of the last SSE performed (last months versus longer); or d) the frequency of SSE (how many

times or how often was SSE conducted individually, with a partner, or with tracking/monitoring. Of note, no two trials assessed SSE using identical methods. Last, after surveilling all of the sources (references) cited in the method sections of the 12 trials, we found minimal evidence supporting the validity and reliability of the items used to assess SSE in these trials. There are several key messages directly emerging from this study. First, we confirmed that there currently is no standardized method to assess SSE. There was some variability in the modalities used to assess SSE across studies, which makes the comparability of results from such studies difficult. Second, there is an urgent need for research studies to investigate the validity of the assessment methods used for SSE. It is noteworthy that the task of establishing the validity and reliability of SSE measures poses many difficulties. First, SSE is a patient-reported outcome, which is affected by reporting bias. Second, for the purpose of establishing construct validity, there is no hard outcome to compare SSE against. The construct validity of an SSE scale could be established in the future via a Delphi study where melanoma prevention experts (dermatologists, primary care physicians, and researchers, including methodologists) and patients could aim to reach consensus on the most relevant items. Third, the next step in establishing the validity of the SSE scale would be to evaluate the association of SSE behaviour with health outcomes, such as mortality/survival and melanoma early detection. Such a relationship is difficult to evaluate in the absence of a reliable scale to measure SSE behavior. But the validity of the SSE behavior scale partially depends on establishing a consistent relationship between SSE behavior and other relevant/health outcomes.

The main limitation of this study is that we only reviewed randomized controlled trials and we excluded studies with any other study design. We intended to review studies with the most rigorous design (RCT), with the assumption that these well-resourced studies would be most likely to assess the main outcomes with reliable and valid instruments. While there is a chance that we might have missed some studies, which operationalized SSE differently than the modalities used in the RCTs included in our review, it is highly unlikely that this would have changed the final conclusions about the lack of a standardized method to measure SSE being representative of the melanoma prevention field. An international research collaboration is currently

underway with the COMET Initiative (http://www.comet-initiative.org/) to compile a comprehensive list of patient-reported outcomes to be used in melanoma intervention research, which ideally would include SSE.

The aim of the second manuscript was to provide a comprehensive and replicable review of the evidence to date for intervention strategies that promote skin self-examination and to determine if interventions that are effective at skin checking behaviours are also resulting in early detection and decreased melanoma-related mortality. The methodology of this review, including the search strategy and study selection criteria, was identical to that of the first study. The second study investigated the effect of behavioural interventions on three outcomes (melanoma-related mortality, melanoma early detection, and melanoma preventive behaviours, such as skin exams) among populations at an increased risk for melanoma. None of the 12 trials included in this review investigated mortality or early detection, but all evaluated the impact of interventions on melanoma preventive health behaviours, such as skin self-exams (SSE), partner-assisted skin exams (PASE), or clinician administered skin exams (CSE). Seven trials compared an active intervention against a non-active control and 5 trials compared an active intervention against an active control. All of the 12 trials recommended that SSE be conducted, and some clearly specified that the ABCDE criteria be used, which includes checking moles for asymmetry, border irregularity, colour differences within one mole, diameter > 5 mm, and evolution (or changes) of any of these parameters. Most trials included recommendations for SSE in pamphlets, but in a few cases, standardised live demonstrations and videos of a skin exam were also provided to participants. Some trials included additional intervention components, such as psychological counselling sessions to address barriers to screening, genetic counselling sessions, or clinical skin exams performed by physicians with the possibility for participants to ask questions about skin checking. We found some methodological heterogeneity between the trials, with respect to intervention components and the methods used to assess the behavioural outcomes. In particular, the trials that used continuous scoring for the behavioural outcomes used different ranges to assess the behaviours. Also, the trials that compared two active interventions used different strategies to promote SSE which made their over results impossible to pool in a meta-analytic approach. Among the trials that allowed for between-trial comparison and pooling of effects (i.e., comparing an active intervention versus a

non-active control and using binary outcomes measures), we computed a random effects meta-analysis, which showed a small significant effect on SSE but a non-significant effect on PASE or CSE. Our findings show that providing individuals at increased risk for melanoma with personalized information about their melanoma risk and detailed instructions on how to perform a skin self-exam in order to identify problematic lesions is a superior approach to the current standard of care, which involves generic statements about risk for melanoma and brief recommendations for SSE, delivered verbally or via a generic melanoma prevention pamphlet. Our review also identified incomplete reporting procedures across most trials and in some cases, low power and/or small sample sizes. The key messages from this review are that interventions aiming to improve adherence to SSE seem to be successful when tailored to individual prevention needs. Clinical trials testing behavioural interventions in at-risk groups for melanoma would benefit from improved reporting practices (e.g., detailed description of study procedures, such as randomization or blinding, management of missing data) and improved methodological rigor (e.g., preregistration of the study, including primary outcomes, data analysis plan, and the plan for managing attrition). Lastly, randomized controlled trials might not be the most feasible design to use in order to answer the questions of whether behavioural interventions targeting SSE could in fact contribute to melanoma early detection and reductions in mortality rates. Studies investigating these outcomes require large sample sizes and follow-ups longer than 12 months. For example, in order to compare detection rates among those exposed to an intervention versus control, it would require that a significant number of people get diagnosed with melanoma in both conditions. Among people at highest risk for melanoma, i.e., with a personal history of melanoma, the second primary melanoma is likely to develop within 10 years of the first diagnosis for individuals > 55 years of age and within 5 years of the first diagnosis for older individuals (Jones et al., 2016). Appropriate follow-ups for studies investigating melanoma early detection among melanoma survivors should be set at 5-10 years. Further, it is very difficult, if not impossible, to design a control group that has no exposure to information about SSE, since that information has been readily available in the media since the 1970s. Furthermore, for individuals at high-risk, such as melanoma survivors, recommendations for SSE are part of the best practice care, so it would be unethical to randomize only some of these individuals

to an active intervention that educates about the benefits of and teaches the specifics of SSE. A more suitable, feasible, and ecological design could be a cohort or observational study with longitudinal follow-up which would allow for data to be gathered from significantly larger sample sizes over longer periods of time without the associated costs attributed to conducting a randomized trial.

The main limitation of this systematic review, which is shared between manuscripts 1 and 2, is that we only reviewed randomized controlled trials and we excluded studies with any other study design. The RCT design is best positioned to answer our research questions about the efficacy of behavioural interventions in promoting melanoma prevention behaviours. However, it should be noted that due to limited follow-up, the studies included in our review most likely captured the uptake of the health behavior, but not the maintenance of the health behaviour change, which are arguably different phases (or stages) in the adoption of a new health behaviour (Prochaska & Velicer, 1997).

The aim of the third manuscript was to identify short- and long-term predictors of SSE following best-practice care, which included an educational session on how to perform SSE in a sample of individuals diagnosed with melanoma. Short-term adherence to SSE was assessed at 3 months post the educational session and long-term adherence to SSE was assessed at 12- and 24-months post. We assessed SSE behavior in two different ways: the comprehensiveness of a skin exam (as the extent of the body covered by the skin exam; the body was split into 5 parts) and optimal SSE (as monthly checking of the 5 body parts, as per recommendations provided during the educational session). We found that both the comprehensiveness and the optimal performance decreased over time. Intentions to perform SSE was the strongest predictor of comprehensiveness of the exam at short and long-term follow-ups. SSE intentions and SSE self-efficacy were the strongest predictors of optimal SSE at 3 months follow-up and SSE self-efficacy continued to be the strongest predictor of optimal SSE at 24 months follow-up while SSE intentions were not. To our knowledge, this is the first study in the literature to address the short- (3 months) and long-term (12 and 24 months) predictors of SSE behaviour in a sample of melanoma patients receiving ongoing follow-up care. The main limitations of the study include weaknesses specific to the longitudinal design: loss to follow-up affected the

precision of our estimates, especially at the final time point (24 months post). Further, we assessed SSE behaviour via self-report measures, which is subject to response bias. Furthermore, we created the SSE measure based on items previously used in the literature, but our measure has not been validated with an external sample. Future longitudinal studies might incorporate technological devices (e.g., electronic applications) to assist with skin surveillance, which might also record the frequency and thoroughness of the skin exam in real time. Future studies should also explore the validity of our SSE measures in other independent samples.

Conclusions

Manuscript 1 found that there is no standardized method of assessing SSE in behavioural trials conducted with individuals at increased risk for developing melanoma. Future research is needed to identify a unified definition of a skin exam and a standardized method to assess SSE behaviours in clinical trials. Manuscript 2 found that there are a few interventions that are efficacious at improving SSE behaviour. Future clinical trials involving behavioural interventions with individuals at increased risk for melanoma should use improved reporting procedures and trials should be registered ahead of time. Manuscript 3 found that in the short and long-term, intentions to perform SSE predicted the comprehensiveness of SSE (extent of body covered by the skin exam) and self-efficacy for SSE predicted adherence to optimal SSE (monthly checking of entire body). These results have implications for the design of future melanoma prevention interventions, as intentions for SSE and self-efficacy for SSE are highly amenable to change and can be easily targeted by psycho-social intervention with at-risk people.

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