BMJ Open

Impact of alternative diagnostic labels for melanoma in-situ on management choices and psychological outcomes: An online randomised study.

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2024-089558
Article Type:	Protocol
Date Submitted by the Author:	03-Jun-2024
Complete List of Authors:	Wu, Zhuohan; The University of Sydney, Sydney School of Public Health, Faculty of Medicine and Health Elder, David; Hospital of the University of Pennsylvania, Department of Pathology and Laboratory Medicine Ferguson, Peter M.; Melanoma Institute Australia; Royal Prince Alfred Hospital and NSW Health Pathology, Tissue Pathology and Diagnostic Oncology O'Brien, Blake; Sullivan Nicolaides Pathology, Surgical Pathology Barnhill, Raymond; Paris Sciences and Lettres Research University, Department of Translational Research van Akkooi, Alexander C.J.; Melanoma Institute Australia Low, Donald; Cancer Voices New South Wales Low, Cynthia; Cancer Voices New South Wales Davies, Elspeth; Patient Researcher, Cambridge Liu, Sherrie; Health Consumers New South Wales Lewis, Stacey; Health Consumers New South Wales Spongberg-Ross, Bella; Health Consumers New South Wales Bell, Katy; The University of Sydney; Wiser Healthcare Research Collaboration Nickel, Brooke; University of Sydney, Sydney School of Public Health, Faculty of Medicine and Health; Wiser Healthcare Research Collaboration boroumand, farzaneh; The University of Sydney Scolyer, Richard; The University of Sydney Adamson, Adewole S.; Austin, Department of Internal Medicine; The University of Texas at Austin Dell Medical School, Emery, Jon; University of Melbourne, General Practice and Primary Care Academic Centre Parker, Lisa; University of Sydney
Keywords:	Dermatological tumours < DERMATOLOGY, Adverse events < THERAPEUTICS, Clinical Decision-Making, Surgical dermatology < DERMATOLOGY, Surgical pathology < PATHOLOGY, Patient-Centered Care

Impact of alternative diagnostic labels for melanoma in-situ on management choices and psychological outcomes: An online randomised study.

Zhuohan Wu[1], Brooke Nickel[1,2], Farzaneh Boroumand[1,3], David Elder[4], Peter Ferguson[5,6], Richard A. Scolyer[5,6,7,8], Blake O'Brien[9], Raymond Barnhill[10], Adewole S Adamson[11], Alexander C.J. van Akkooi[5,12], Jon Emery[13], Lisa Parker[14,15], Donald Low[16], Cynthia Low[16], Elspeth Davies[17], Sherrie Liu[18], Stacey Lewis[18], Bella Spongberg-Ross[18], Katy JL Bell[1,2]

[1]Sydney School of Public Health, Faculty of Medicine and Health, The University of Sydney, Sydney, Australia.

[2] Wiser Healthcare Research Collaboration, Sydney, NSW, Australia

[3] School of Mathematical and Physical Sciences, Macquarie University, NSW, Australia

[4] Department of Pathology and Laboratory Medicine, Hospital of the University of Pennsylvania, Philadelphia

[5] Melanoma Institute Australia, The University of Sydney, Sydney, NSW, Australia

[6] Tissue Pathology and Diagnostic Oncology, Royal Prince Alfred Hospital and NSW Health Pathology, Sydney, NSW, Australia

[7] Faculty of Medicine and Health, The University of Sydney, Sydney, NSW, Australia

[8] Charles Perkins Centre, The University of Sydney, Sydney, NSW, Australia

[9] Sullivan Nicolaides Pathology, Brisbane, QLD, Australia

[10] Department of Translational Research, Institut Curie, Paris Sciences and Lettres Research University, and Faculty of Medicine University of Paris Descartes, Paris, France

[11]Department of Internal Medicine (Division of Dermatology), The University of Texas at Austin Dell Medical School, Austin, TX 78701, USA

[12] Royal Prince Alfred Hospital, Department of Melanoma and Surgical Oncology,

[13] Centre for Cancer Research, University of Melbourne, Melbourne, VIC, Australia

[14] School of Pharmacy, Faculty of Medicine & Health, Charles Perkins Centre, University of Sydney, Australia

[15]Department of Radiation Oncology, Royal North Shore Hospital, Sydney, Australia

[16] Cancer Voices New South Wales, NSW, Australia

[17] Patient Advocate, Cambridge, UK

[18] Health Consumers New South Wales, NSW, Australia

Corresponding Author: Katy Bell katy.bell@sydney.edu.au

Abstract

Introduction

A diagnosis of melanoma in-situ presents negligible risk to a person's lifespan or physical wellbeing, but existing terminology makes it difficult for patients to distinguish these from higher risk invasive melanomas. This study aims to explore whether using an alternative label for melanoma in situ may influence patients' management choices and anxiety levels.

Methods and Analysis

This study is a between-subjects randomised online experiment, using hypothetical scenarios. Following consent, eligible participants will be randomised 1:1:1 to three labels: "melanoma in situ" (control), "low-risk melanocytic neoplasm" (intervention 1) and "low-risk melanocytic neoplasm, in situ" (intervention 2). The required sample size is 1668 people. The co-primary outcomes are (i) choice between no further surgery or further surgery to ensure clear histological margins greater than 0.5mm, and (ii) choice between patient initiated clinical follow up when needed (patient-led surveillance) and regular routinely scheduled clinical follow-up (clinician-led surveillance). Secondary outcomes include diagnosis anxiety, perceived risk of invasive melanoma and of dying from melanoma, and management choice anxiety (after surgery choice and follow-up choice). We will make pairwise comparisons across the three diagnostic label groups using regression models (univariable and multivariable).

Ethics and Dissemination

The study has been registered with the Australian New Zealand Clinical Trials Registry (ACTRN12624000740594). Ethics approval has been received from The University of Sydney Human Research Ethics Committee (2024/HE000019). Results of the study will be published in a peer-reviewed medical journal and a plain language summary of the findings will be shared on the Wiser Healthcare publications page https://www.wiserhealthcare.org.au/category/publications/.

Strengths and Limitations of This Study

- The randomised design will provide highly relevant evidence on potential impacts of alternative diagnostic labels for melanoma in situ to patients' decision-making and psychological outcomes.
- The study has been co-designed with consumers and clinicians to ensure labels and evidence are relevant to end-users.
- The large online randomised study will be representative of adults in the Australian community.
- The hypothetical nature of the study means it cannot capture experiences of patients after an actual melanoma in situ diagnosis, nor the impact on potential patients' loved ones.
- The study does not explore the potential for recalibration of diagnostic thresholds using existing labels. This is an important area for further research.

INTRODUCTION

Melanoma incidence and mortality trajectories in Australia and other countries show a classic epidemiologic signature of overdiagnosis[1]: steeply increasing incidence curves coupled with flat mortality trends[2-6]. While aging populations may lead to a small real increase in melanoma incidence[7], much of the increase is likely overdiagnosis[2-6].[2-6]. This appears to be largely driven by increased diagnosis of melanoma in situ[2 4 8], which in Australia is now diagnosed over twice as frequently as invasive melanoma[9]. Similar findings have been found for melanoma in the US (diagnosed at least as frequently as invasive melanoma)[3] and Denmark (diagnosed over half as frequently as invasive melanoma)[10].

Multiple evidence lines indicate that melanoma in situ is a risk factor for invasive melanoma rather than an obligate precursor[3 9 11 12].[3 9 11 12]. Overdiagnosis is partly driven by lowering the diagnostic threshold over the years, such that the same lesion that was called benign in the past, would now be labeled melanoma in situ[12]. Concerns about litigation may also be driving a tendency to interpret melanocytic lesions as a more severe diagnosis[13] particularly in partial biopsies or where the lesion extends to the surgical margins. Harms stemming from melanoma overdiagnosis include physical, psychosocial, and economic dimensions[14]. Physical harms can include overtreatment, repeat skin biopsies[15], scarring[15], pain, infection, and/or functional impairment. Psychological harms include anxiety and fear[16 17], with many

patients perceiving they have a high risk of dying from melanoma, when their actual risk is much lower (and risk all-cause mortality is actually lower than the population average)[18]. These psychological harms can manifest as anxiety about being outdoors, fear of cancer recurrence, or guilt for past UV exposure causing melanoma[5]. Social harms include impacts of the diagnosis on loved ones, and on patients' social networks[15]. Economic harms include treatment costs for the immediate diagnosis, and for future long term clinical surveillance. These incur substantial financial costs to both the health system and patient (as out-of-pocket costs), as well as opportunity costs for both clinician time and patient time. There is also a possible denial of life insurance as the person is now identified as a cancer survivor by many insurance companies (3).

One possible solution is to consider a new label for melanoma in situ without the word "melanoma"[12]. This might help patients recognize the lower risk of this type of lesion[18], and help to reduce the potential psychological harm. It may also pave the way for the de-escalation of treatment [19] and surveillance[20-22]. Evidence from other cancer contexts, including thyroid[23], breast[24], and prostate[25] lesions, suggests that new diagnostic labels may beneficially impact psychological outcomes and management decisions[26]. We seek to build on these findings by investigating the potential impacts of new labels for melanoma in situ. To ensure relevance of our findings to end-users, we will test alternative labels for melanoma in situ that were chosen by our co-

Investigators representing clinicians, patients, and the public. Alternative label(s) need to be acceptable to both patients and clinicians, and convey the low, but not zero, risk of future invasive melanoma. This study aims to explore whether using an alternative diagnostic label to communicate a hypothetical melanoma in situ diagnosis influences management choice and level of anxiety among Australian adults.

METHODS AND ANALYSIS

Study design

An online randomised study of Australian community members will be run, with, participants randomised to receive one of three hypothetical scenarios about the diagnosis of a melanoma in situ. Each group will be presented with a different diagnostic label, and we will survey participants about their preferred choices of management for that diagnosis, their level of anxiety about that diagnosis and their level of anxiety about their management choices.

This study is a between-subjects randomised online experiment. Following consent, eligible participants will be randomised 1:1:1 to “melanoma in situ” (control), “low risk melanocytic neoplasm” (intervention label 1), and “low risk melanocytic neoplasm, in situ” (intervention label 2). The co-primary outcomes and secondary outcomes will be compared across randomised groups.

There will be an equal probability of being assigned to each of the 3 groups, and we expect approximately equal numbers per group. We will use Qualtrics survey

software to randomly allocate participants into groups, present the scenarios, survey questions and collect data on the outcomes (Qualtrics, Provo, UT, 2020). Our participants flow diagram present a summary of the randomisation of participants into the allocated control and intervention arms (Figure 1).

Eligibility criteria

Participants will be eligible if they are: 40 years or older, understand written English, and reside in Australia. Participants will be excluded if they have a history of melanoma (invasive or in-situ).

Recruitment and data collection.

Participants will be recruited via Qualtrics. Participants who agree to participate in the study will complete an online Qualtrics survey managed by the research team. Only eligible participants will proceed to the randomisation step. The survey will capture baseline data and characteristics of participants including socio-demographic details including their age, location, health literacy, and personal and family history of any cancer, and participant responses on outcome measures. The survey questions are presented in the Supplement.

All data will be collected via Qualtrics software and hosted on The University of Sydney secure server. Information will be de-identified and we will not be able to link the survey back to participants. The non-identifiable data will be downloaded for

analysis and stored within The University of Sydney's Research Data Store.

Determination of alternative labels to be tested.

We undertook a targeted literature search in September 2023 by retrieving forward and backward citation searches of four key papers on the topic (10,15,16,21). We used the automated tool 'Spider Cite' (22) to identify records, and Covidence to to screen title, abstract and full-texts (Veritas Health Innovation, Australia; https://www.covidence.org). Of 593 unique records retrieved, we screened the full text of 27, and included 7 papers describing 9 alternative labels (see Box 1). Using short online questionnaires implemented in Qualtrics (Provo, UT: Qualtrics, 2020), we then ran three rounds of surveys with the 9 international Clinician co-Investigators (with expertise in dermatopathology, dermatology, surgical oncology, primary care, and radiation oncology), and 6 Patient/Public co-Investigators (two with lived experience of a melanoma diagnosis and four without a history of melanoma) to determine choice of alternative labels. This resulted in the final choice of two alternative labels that we will test in the online survey: ***low-risk melanocytic neoplasm*** and ***low-risk melanocytic neoplasm, in situ***.

Interventions

Participants will be randomised using Qualtrics randomisation software to receive one of three hypothetical scenarios. They will not be blinded. In each scenario, the

participant will be told that the results of their recent skin surgery indicates a particular diagnosis. Group 1 (the control group) will be told they have a ***melanoma in situ***. Group 2 will be told they have a ***low-risk melanocytic neoplasm***. Group 3 will be told they have a ***low-risk melanocytic neoplasm, in situ***.

Primary and Secondary Outcomes

Primary and secondary outcomes are described in Table 1. The co-primary outcomes are (i) participant's choice of surgical management option: no further surgery vs further surgery, and (ii) follow-up management option: patient led surveillance (self-skin examination with patient-initiated clinic visits) vs clinician led surveillance (six monthly routinely scheduled clinic visits). Secondary outcomes are: diagnosis anxiety, perceived lifetime risk of invasive melanoma, perceived lifetime risk of dying from melanoma, management choice anxiety, and open-text explanation of management choices (free text input).

Sample size

We estimated a sample size of 1668 participants with 556 participants per group in the study, which would provide 80% power (1 - β) to detect a pairwise difference in the proportion of choosing no further surgery, and 89% power to detect a pairwise difference in the proportion in choosing patient-led surveillance as small as 10%. The assumptions are: 50% would choose no further surgery (most conservative

assumption) and 35%[22] would choose patient-led surveillance in the control label condition, a 5% dropout rate, $\alpha = 0.05$, the normal approximation to the binomial distribution, and the standard formula for comparing proportions in independent equal-sized groups.

Analysis

The analysis will focus on assessing the impact of different diagnostic labels for melanoma in situ on participants' psychological responses and healthcare decisions. Data analysts will be blinded to intervention assignment. For both co-primary outcomes, we will compare the proportion chosen for each management option. For first four secondary outcomes, we will compare summary statistical measures (means or medians) across randomised groups. For the last outcome, we will use thematic framework methods of qualitative data.

The analysis will adhere to the intention-to-treat principle, and participant data will be analyzed according to their randomly assigned diagnostic label group, regardless of adherence to the study protocol. The number of participant responses included in each analysis will be presented for each outcome. We will summarize categorical data for the randomised groups using counts and percentages, and continuous data using the minimum and maximum, mean, and standard deviation (SD) or median and interquartile range (IQR).

Statistical analyses will be conducted within a superiority framework to make pairwise comparisons across the three diagnostic label groups. Binary outcomes will be analyzed using logistic regression. Continuous outcomes will be analyzed using linear regression. For the cancer worry outcome, we will compare changes in worry across randomised groups by including baseline scores as a covariate in the regression model. Effect estimates for all primary and secondary outcomes will be presented with associated 95% confidence intervals (CI). All hypothesis tests will be two-sided with a significance level (α) of 5%. The potential for participants' health literacy to act as an effect modifier of intervention effects will be explored.

We will estimate unadjusted and adjusted effects using the relevant regression model. These will include variables used in sampling strata: age, education, geographic location (by state/territory). Prognostic factors will be measured through the baseline questionnaire, and include baseline anxiety levels, sun exposure behavior, prior diagnosis of melanoma, diagnosis of melanoma in a family member. The effects of participants' health literacy on intervention effects will also be explored as a potential confounder.

Patient and public involvement

Two authors have lived experience of a melanoma diagnosis, and four authors are

members of the public. Two authors are affiliated with Cancer Voices NSW, one author is a patient researcher from Cambridge UK, and three authors are affiliated with Health Consumers NSW.

Ethics and Dissemination

Ethics approval of this project was provided by the University of Sydney on 06 May 2024 (No. 2024/HE000019). The study is registered with the Australian New Zealand Clinical Trials Registry (ID 386943). Updates to the protocol will be uploaded to the registry and identified by version number.

As this study is an online randomised experiment which includes a hypothetical scenario, we do not anticipate significant adverse events because of the trial interventions or conduct. Participants are reminded at several points before and after the study as part of the participant information, consent and debrief processes that the nature of the study is hypothetical, that none of the information relates to their actual health or wellbeing, and that researchers do not have access to their actual medical histories or information. The debriefing content also includes links to relevant resources for participants who wish to find out more.

The research team will have access to the final dataset. Access may be granted to other researchers on reasonable request. No contractual agreements limit the disclosure of data to other investigators. The findings of the study will be published in a peer-reviewed medical journal. A lay summary of the findings will be published via

permanent link at the Wiser Healthcare publications page.

Conclusion

This research protocol outlines a study that aims to investigate the impact of alternative diagnostic labels for melanoma in situ on healthcare decisions and psychological outcomes. The study was designed in accordance with SPIRIT guidelines and will be conducted in line with CONSORT guidance.

The potential significance of this study lies in its ability to impact clinical practice and policy by identifying alternative diagnostic labels for melanoma in-situ that are acceptable to patients, pathologists, and treating clinicians. Widespread adoption of new labels for low-risk melanocytic lesions that do not include the word "melanoma", may mitigate the harms from overdiagnosis and overtreatment. Alternative labeling of melanoma in-situ may better inform patients about the low level of risk associated with the lesion, and allow appropriate de-escalation of treatment and surveillance options.[18] This would lessen burdens on individuals, their loved ones, clinicians, and health systems. Results may also provide evidence relevant to other low-risk conditions.

Contributors

ZW co-led drafting of the manuscript, led drafting of the study questionnaire and application to the Human Research Ethics Committee, and assisted with the targeted

literature review (full text screening and data extraction). BN and KB conceptualized the research, provided methodological expertise, and revised the manuscript draft. KB led the targeted literature review and the Clinician and Consumer Investigator survey to decide the choice of alternative labels, and co-led drafting of the manuscript. FB calculated the sample size. All authors read, contributed to, and approved the final manuscript.

Funding

Funding for the study is provided by a National Health and Medical Research Council of Australia (NHMRC) Centre for Research Excellence Grant (2021/GNT2006545). Brooke Nickel is supported by a NHMRC Investigator Grant (2020/GNT1113532). RAS is supported by a NHMRC Investigator Grant (2022/GNT2018514). Katy Bell is supported by a NHMRC Investigator Grant (2019/GNT1174523). The University of Sydney is the Sponsor of the study. The funder and sponsor had no role in the study design, collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication.

Declaration of Interests

RAS has received fees for professional services from SkylineDx BV, IO Biotech ApS, MetaOptima Technology Inc., F. Hoffmann-La Roche Ltd, Evaxion, Provectus Biopharmaceuticals Australia, Qbiotics, Novartis, Merck Sharp & Dohme, NeraCare,

AMGEN Inc., Bristol-Myers Squibb, Myriad Genetics, GlaxoSmithKline.

AvA received Advisory Board/Consultancy Honoraria from 4SC AG, Amgen, Bristol-Myers Squibb, Merck Serono-Pfizer, MSD-Merck, Neracare, Novartis, Pierre Fabre, Sanofi, Sirius Medical, SkylineDX and Research Grants from Amgen, Merck Serono-Pfizer, SkylineDX.

All other authors have no conflicts of interest to declare.

References:

1. Welch HG, Kramer Barnett S, Black William C. Epidemiologic Signatures in Cancer. New England Journal of Medicine 2019;381:1378-86.

2. Glasziou PP, Jones MA, Pathirana T, et al. Estimating the magnitude of cancer overdiagnosis in Australia. Med J Aust 2020;212:163-68.

3. Welch HG, Mazer BL, Adamson AS. The Rapid Rise in Cutaneous Melanoma Diagnoses. N Engl J Med 2021;384:72-79.

4. Adewole SA, Geetanjali N, Mark AJ, et al. Ecological study estimating melanoma overdiagnosis in the USA using the lifetime risk method. BMJ Evidence-Based Medicine 2024:bmjebm-2023-112460.

5. Adamson AS, Suarez EA, Welch HG. Estimating Overdiagnosis of Melanoma Using Trends Among Black and White Patients in the US. JAMA Dermatol 2022;158:426-31.

6. Mille Falk B, Emma Grundtvig G, John Brandt B. Overdiagnosis in malignant melanoma: a scoping review. BMJ Evidence-Based Medicine 2024;29:17.

7. Long GV, Swetter SM, Menzies AM, et al. Cutaneous melanoma. The Lancet 2023;402:485-502.

8. Whiteman DC, Olsen CM, MacGregor S, et al. The effect of screening on melanoma incidence and biopsy rates. Br J Dermatol 2022;187:515-22.

9. Olsen CM, Pandeya N, Rosenberg PS, et al. Incidence of in Situ vs Invasive Melanoma: Testing the "Obligate Precursor" Hypothesis. J Natl Cancer Inst 2022;114:1364-70.

10. Nielsen JB, Kristiansen IS, Thapa S. Increasing melanoma incidence with unchanged mortality: more sunshine, better treatment, increased diagnostic activity, overdiagnosis or lowered diagnostic threshold? Br J Dermatol 2024:ljae175.

11. Elder DE. Obligate and Potential Precursors of Melanoma. J Natl Cancer Inst 2022;114:1320-22.

12. Semsarian CR, Ma T, Nickel B, et al. Do we need to rethink the diagnoses melanoma in situ and severely dysplastic naevus? Br J Dermatol 2022;186:1030-32.

13. Titus LJ, Reisch LM, Tosteson ANA, et al. Malpractice Concerns, Defensive Medicine, and the Histopathology Diagnosis of Melanocytic Skin Lesions. Am J Clin Pathol 2018;150:338-45.

14. Bell KJL, Nijsten T. Melanoma overdiagnosis: why it matters and what can be done about it. Br J Dermatol 2022;187:459-60.

15. Elspeth D. Informed by research, transformed by research. BMJ Evidence-Based Medicine 2024;29:62.

16. Bell KJL, Mehta Y, Turner RM, et al. Fear of new or recurrent melanoma after treatment for localised melanoma. Psycho-Oncology 2017;26:1784-91.

17. Mahama AN, Haller CN, Labrada J, et al. Lived Experiences and Fear of Cancer Recurrence Among Survivors of Localized Cutaneous Melanoma. JAMA Dermatol 2024;160:495-501

18. Patel VR, Roberson ML, Pignone MP, et al. Risk of Mortality After a Diagnosis of Melanoma In Situ. JAMA Dermatology 2023;159:703-10.

19. Zijlker LP, Eggermont AMM, van Akkooi ACJ. The end of wide local excision (WLE) margins for melanoma ? European Journal of Cancer 2023;178:82-87.

20. Moncrieff MD, Bastiaannet E, Underwood B, et al. Follow-up Schedule for Patients With Sentinel Node–negative Cutaneous Melanoma (The MELFO Study): An International Phase III Randomized Clinical Trial. Annals of Surgery 2022;276: e208-e216.

21. Lim W-Y, Morton RL, Turner RM, et al. Patient Preferences for Follow-up After Recent Excision of a Localized Melanoma. JAMA Dermatology 2018;154:420-27.

22. Drabarek D, Ackermann D, Medcalf E, et al. Acceptability of a Hypothetical Reduction in Routinely Scheduled Clinic Visits Among Patients With History of a Localized Melanoma (MEL-SELF): Pilot Randomized Clinical Trial. JMIR Dermatol 2023;6:e45865.

23. Nickel B, Barratt A, McGeechan K, et al. Effect of a Change in Papillary Thyroid Cancer Terminology on Anxiety Levels and Treatment Preferences: A Randomized Crossover Trial. JAMA Otolaryngol Head Neck Surg 2018;144:867-74.

24. McCaffery K, Nickel B, Moynihan R, et al. How different terminology for ductal carcinoma in situ impacts women's concern and treatment preferences: a randomised comparison within a national community survey. BMJ Open 2015;5:e008094.

25. Berlin A, Ramotar M, Santiago AT, et al. The influence of the "cancer" label on perceptions and management decisions for low-grade prostate cancer. JNCI: Journal of the National Cancer Institute 2023;115:1364-73.

26. Nickel B, Moynihan R, Barratt A, et al. Renaming low risk conditions labelled as cancer. BMJ 2018;362:k3322.

Box 1: Process to select alternative labels to melanoma in situ for testing

• In the first-round surveys Clinician and Patient/Public co-Investigators indicated their ranking the 7 labels identified in the targeted literature search, and 2 additional labels in order of preference. The potential alternative labels from the literature search were: Melanocytic neoplasm of low malignant potential (8,24,25), Melanocytic neoplasm, Atypical neoplasm" (25), Severe or High-Grade Melanocytic Dysplasia, Superficial Atypical Melanocytic Proliferation of Uncertain Malignant Significance (SAMPUS) (26–28), Melanocytic Tumor of Uncertain Malignant Potential (MELTUMP), Melanocytoma (28). The two additional labels suggested by the research team were: low-risk melanocytic neoplasm and low-risk melanocytic lesion.

• In the second round surveys, co-Investigators indicated their preferred ranking of the top three choices from round 1 and two new labels suggested in round 1: Low-risk melanocytic neoplasm, Low-risk melanocytic lesion, and Melanocytic neoplasm of low malignant potential, Melanocytic intraepithelial neoplasia, and In situ melanocytic neoplasm.

• In the third round surveys, co-Investigators indicated their preferred ranking of the top two choices from round 2, and three new labels suggested in round 2: In situ melanocytic neoplasm, Low-risk melanocytic neoplasm, In situ melanocytic neoplasm, low risk, low-risk melanocytic neoplasm, in-situ, and dysplastic naevus. The two highest ranked labels, chosen as the alternative labels to test in the online

experiment, were: "***low-risk melanocytic neoplasm***" and "***low-risk melanocytic neoplasm, in-situ***".

384

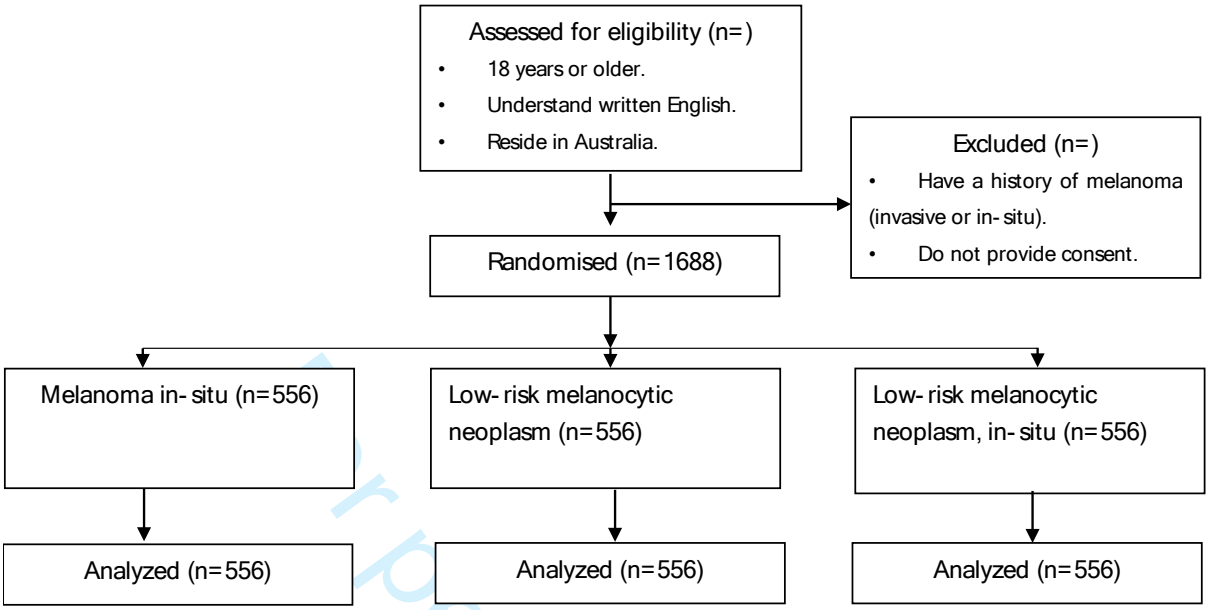
Table 1. Participant characteristics and outcome measures.

Variable	Measure
Participant Characteristics	
Melanoma risk	Melanoma risk prediction based self-assessed risk factors[27]
General mood and wellbeing.	WHO (Five) Well-Being Questionnaire.[28]
Medical minimiser/maximiser.	Single-Item Maximiser/Minimiser Elicitation Question (MM1).[29]
Health literacy.	Single Item Literacy Screener (SILS).[30]
Melanoma worry.	Direct choice between specified options, one choice possible.
Self-efficacy.	Generalized Self-Efficacy Scale (GSE).[31]
Primary Outcomes	
Co-primary outcomes are choices for two management decisions. 1. Choice of further surgery: • No further surgery • Further surgery to ensure margins >0.5mm from lesion on pathology 2. Choice of follow-up: • Patient led surveillance: self-monitoring with patient-initiated clinic visits as needed • Clinician led surveillance: six monthly routinely scheduled clinic visits	Direct choice between two management approaches for each co-primary outcome Choice of further surgery and choice of follow-up.
Secondary Outcomes	
Diagnosis anxiety.	Single-question Visual Analogue Scale (0-10).[32]
Perceived lifetime risk of invasive melanoma	Single-question Visual Analogue Scale (0-100)
Perceived lifetime risk of dying from melanoma	Single-question Visual Analogue Scale (0-100)

Management choice anxiety.	Single-question Visual Analogue Scale (0-10).[32]
Open-text explanation of management choice.	Free text (optional)

386

Figure 1. Study CONSORT flow diagram



Landing Page ✓

Effect of the label for a low risk melanocytic lesion on preferred management strategy: a randomised experiment.

Thank you for your interest in our study about low-risk melanocytic lesion.

In this study, you will be randomised to be shown one of three hypothetical scenarios following surgery on a mole, which will be followed by questions about management options and anxiety.

The study is being conducted by a team of researchers from The University of Sydney School of Public Health. The team members are:

- Professor Katy Bell (School of Public Health at the University of Sydney)
- Dr Brooke Nickel (School of Public Health at the University of Sydney)
- Mr Zhuohan Wu (School of Public Health at the University of Sydney)

Taking part in the study involves completing one online questionnaire which will take approximately 10 minutes to complete.

Being in this study is completely voluntary and you do not have to take part. Your decision on whether to participate will not affect your current or future relationship with the researchers or anyone else at the University of Sydney.

Please take the time to read through the Participant Information Statement below.

If you are interested in taking part in this study, you will be asked to consent to take part by ticking the 'yes' box at the beginning of the questionnaire. By giving your consent to take part in this study, you are telling us that you:

✓ Understand what you have read in the Participant Information Statement.
✓ Agree to take part in the research study as outlined in Participant Information Statement.
✓ Agree to the use of your personal information as described.

When you have consented, you will fill out an online questionnaire that asks a series of questions, such as:

- Demographic questions, such as age, education, income level and relationship status.
- General health and cancer related questions.
- Melanoma and other cancer history related questions.

You will be randomised to read one of three HYPOTHETICAL EXAMPLES (these are made up examples) in which different labels are used to explain a low-risk melanocytic skin lesion result. **Please note that you WILL NOT be receiving information or advice on any real mole check results or information about your actual health status**.

The hypothetical examples will be followed by questions about choice of management strategy and personal perspective.

Pre-Survey PIS ✓

Effect of the label for a low-risk melanocytic lesion on management strategy: a randomised experiment

PARTICIPANT INFORMATION STATEMENT

(1) What is the study about?

You are invited to participate in a study that assesses how different labels given to an atypical mole (low-risk melanocytic skin lesion) affect a person's anxiety and cancer concern, and their intention to undergo different treatment options. We are interested in a range of views and experiences.

(2) Who is running the study?

The study is being conducted by a team of researchers and clinicians.

The team members are:

• Professor Katy Bell (School of Public Health at the University of Sydney).

• Dr Brooke Nickel (School of Public Health at The University of Sydney).

• Mr Zhuohan Wu (School of Public Health at the University of Sydney).

Professor Katy Bell is leading the study.

(3) What will the study involve for me?

If you agree to participate, you will complete an online questionnaire asking for some background information about yourself and your medical history. You will be randomised to be shown one of three hypothetical scenarios about low-risk melanocytic lesion results, which will be followed by questions about treatment choice, anxiety and cancer concern. After completing and submitting this questionnaire, there will be no further contact anticipated between yourself and the research team.

(4) How much time will the study take?

The study involves one online questionnaire which will take approximately 10 minutes to complete.

(5) Who can take part in the study?

Eligible participants will be people living in Australia aged 40 years or older with no prior history of melanoma. Participants must read and speak adequate English to be eligible.

(6) Do I have to be in the study? Can I withdraw from the study once I've started?

Being in this study is completely voluntary and you do not have to take part. Your decision whether to participate will not affect your current or future relationship with the researchers or anyone else at the University of Sydney. Submitting your completed questionnaire is an indication of your consent to participate in the study. You can withdraw your responses any time before you have submitted the questionnaire without giving a reason. Once you have submitted it, we will not be able to withdraw your responses due to their anonymous nature, and therefore we will not be able to tell which one is yours.

(7) Are there any risks or costs associated with being in the study?

There are no foreseeable risks involved if you participate in this study; however some participants may feel emotional. Participants who express or experience distress during the survey are not obligated to continue and can contact the Cancer Council helpline for support on 13 11 20 or info@cancer.org.au. Please contact researchers via email katy.bell@sydney.edu.au if you require further information or support. Aside from giving up your time, we do not expect that there will be any costs associated with taking part in this study.

(8) Are there any benefits associated with being in the study?

Findings from this study will provide much needed Australian-first data on the impact of different labels for a low-risk melanocytic skin lesion. That said, we cannot guarantee that you will receive any direct benefits from being in the study.

(9) What will happen to the information about me that is collected during the study?

By providing your consent, you are agreeing to us collecting personal information that you provide in your answers to the survey for the purposes of this research study. Your information will only be used for the purposes outlined in this Participant Information Statement, unless you consent otherwise. Your information will be stored securely and your identity/information will be kept strictly confidential, except as required by law. Study findings will be published as articles in academic journals, and presented at conferences, but you will not be individually identifiable in these publications. The research team will have access to the final trial dataset. Access may be granted to other researchers on reasonable request. Sharing research data is important for advancing knowledge and innovation. A de-identified set of the data collected in this study may be made

available for use in future research.

(10) Can I tell other people about the study?

Yes, you are welcome to tell other people about the study.

(11) What if I would like further information about the study?

When you have read this information, Professor Katy Bell will be available to discuss it with you further and answer any questions you may have. If you would like to know more at any stage during the study, please feel free to contact Prof Katy Bell on katy.bell@sydney.edu.au.

(12) Will I be told the results of the study?

You have a right to receive feedback about the overall results of this study. The results of the study and a plain language summary of the findings will be published on the permanent web page wiserhealthcare.org.au/category/publications after the study has been published in a medical journal.

(13) What if I have a complaint or any concerns about the study?

Research involving humans in Australia is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this study have been approved by the HREC of the University of Sydney. As part of this process, we have agreed to carry out the study according to the National Statement on Ethical Conduct in Human Research (2007). This statement has been developed to protect people who agree to take part in research studies. If you are concerned about the way this study is being conducted or you wish to make a complaint to someone independent from the study, please contact the university using the details outlined below. Please quote the study title and protocol number xx.

The Manager, Ethics Administration, University of Sydney:

• Telephone: +61 2 8627 8176

• Email: human.ethics@sydney.edu.au

• Fax: +61 2 8627 8177 (Facsimile)

(14) Has this study received funding?

The study is funded by an NHMRC Centre Research Excellence Grant (2006545, CIA McCaffery) and an NHMRC Investigator Grant (1174523, CIA Bell)

Pre-Survey Consent Form ✓

Do you consent to take part in this study as described in the Participant Information Sheet and Consent Form?

- ◯ Yes
- ◯ No

Section 1: Screening and Socio-Demographic ✓

Which of the following best describes your current gender identity?

- ◯ Male
- ◯ Female
- ◯ Non-binary / gender fluid
- ◯ Different identity

Have you been previously diagnosed with a melanoma?

- ◯ Yes
- ◯ No

Do you have a partner?

- ◯ Spouse

- ◯ De-facto partner
- ◯ Partner who does not reside with you
- ◯ No partner
- ◯ Widowed
- ◯ Divorced or separated
- ◯ [ ] Other - please list:

What is your age?

[ ]

Section 1.5: Screening and Socio-Demographic Part 2

Which Australian state or territory do you currently live in?

- ◯ New South Wales
- ◯ Victoria
- ◯ Australian Capital Territory
- ◯ Queensland
- ◯ South Australia
- ◯ Western Australia
- ◯ Northern Territory
- ◯ Tasmania

Where are you located? (please enter your post code)

[ ]

What is your highest level of education?

- ◯ Year 10 or below
- ◯ Year 11
- ◯ Year 12
- ◯ Certificate I/II
- ◯ Certficate III/IV
- ◯ Advanced diploma/diploma
- ◯ Bachelor's degree
- ◯ Graduate diploma/graduate certificate
- ◯ Postgraduate degree (Master's or Doctorate)
- ◯ Level not determined

What is your current employment status?

- ◯ Permanent or ongoing
- ◯ Fixed-term contract
- ◯ Casual/temporary (no paid sick leave or annual leave)
- ◯ Self-employed
- ◯ On paid leave (e.g. maternity leave)
- ◯ Unemployed
- ◯ Not working/not in the labour force (e.g. student, home duties, retired)

What was your total household income before taxes during the past 12 months?

- ◯ Less than AUD $30,000
- ◯ Between AUD $30,000 - $49,999
- ◯ Between AUD $50,000 - $79,999
- ◯ Between AUD $80,000 - $99,999
- ◯ Between AUD $100,000 - $149,999
- ◯ Between AUD $150,000 - $199,999
- ◯ AUD $200,000 or more
- ◯ Prefer not to say

Do you have children?

- ◯ Yes
- ◯ No
- ◯ Prefer not to say

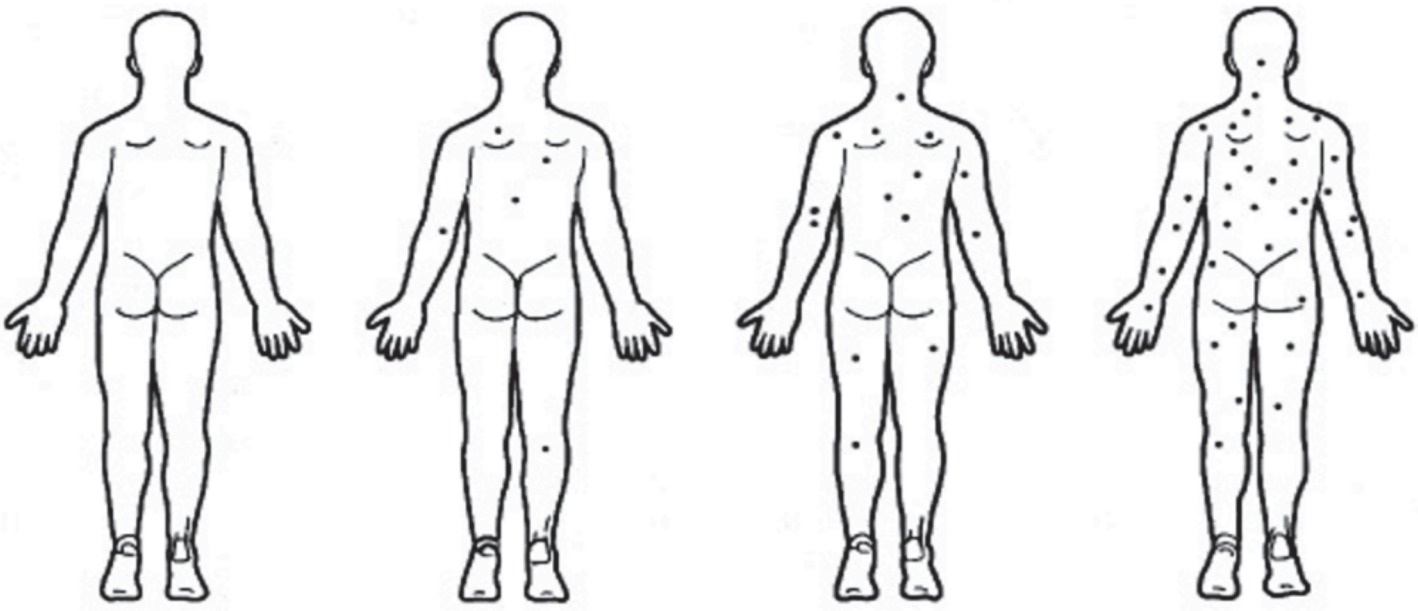
Are you of Aboriginal or Torres Strait Islander origin?

- ◯ Aboriginal
- ◯ Torres Strait Islander
- ◯ Both Aboriginal and Torres Strait Islander
- ◯ Neither Aboriginal or Torres Strait Islander
- ◯ Prefer not to say

What was your natural hair colour when you were 18 years of age

- ◯ Black
- ◯ Brown
- ◯ Fair or Blond
- ◯ Red or Auburn

Looking at the image below, please select the option that most closely resembles the number of moles on your body when you were 18 years of age.



None | Few moles | Some moles | Many moles

- ◯ None
- ◯ Few moles
- ◯ Some moles
- ◯ Many moles

Have you ever used a sunbed or sunlamp?

- ◯ No
- ◯ Yes

Were you born in Australia?

- ◯ Yes
- ◯ No

What is your country of birth?

- ◯ UK
- ◯ India
- ◯ China
- ◯ New Zealand
- ◯ The Philippines
- ◯ [ ] Other - please list:

In which year did you move to Australia?

[ ]

What language do you mostly speak at home?

- ◯ English
- ◯ Mandarin
- ◯ Arabic
- ◯ Cantonese
- ◯ Vietnamese
- ◯ [ ] Other - please list:

Do you have private health insurance?

- ◯ Yes
- ◯ No
- ◯ Don't know

Section 2: General Health ✓

In general, would you say your health is ...

- ◯ Excellent
- ◯ Very good
- ◯ Good
- ◯ Fair
- ◯ Poor

Have you ever been diagnosed with cancer?

- ◯ Yes
- ◯ No
- ◯ Don't know

Which type of cancer?

- ☐ Melanoma
- ☐ Skin (not melanoma)
- ☐ Prostate
- ☐ Breast
- ☐ Bowel
- ☐ Lung
- ☐ Lymphoma
- ☐ _____ Other - please list:
- ☐ Don't know

Has a current or former partner ever been diagnosed with cancer?

- ◯ Yes
- ◯ No

Which type of cancer?

- [ ] Melanoma
- [ ] Skin (not melanoma)
- [ ] Prostate
- [ ] Breast
- [ ] Bowel
- [ ] Lung
- [ ] Lymphoma
- [ ] Other - please list:
- [ ] Don't know

Has anyone in your immediate family (parents, siblings or children) ever been diagnosed with cancer?

- ◯ Yes
- ◯ No
- ◯ Don't know

Which type of cancer? Please tick all that apply

- [ ] melanoma
- [ ] Skin (not melanoma)
- [ ] Prostate
- [ ] Breast
- [ ] Bowel
- [ ] Lung
- [ ] Lymphoma
- [ ] Other - please list:
- [ ] Don't know

Who was this? Please tick all that apply

- ○ Mother
- ○ Father
- ○ Sister
- ○ Brother
- ○ Daughter
- ○ Son
- ○ [ ] Other - please list:

How worried are you about developing melanoma?

- ○ Not worried at all
- ○ A bit worried
- ○ Quite worried
- ○ Very worried

Sometimes, medical action is clearly necessary and sometimes it is clearly not necessary. Other times, reasonable people differ in their beliefs about whether medical action is needed.
In situations where it's not clear, do you tend to lean towards taking action or do you prefer to wait and see if action is needed?
Importantly, there is no right way to be.

I strongly lean towards wait and see.	I lean towards wait and see.	I somewhat lean towards wait and see.	I somewhat lean towards taking action.	I lean towards taking action.	I strongly lean towards taking action.
○	○	○	○	○	○

The following questions are related to how you have been feeling over the past two weeks. Please read each statement and then choose the most appropriate

option regarding how you felt in the last two weeks.

	At no time	Some of the time	Less than half of the time	More than half of the time	Most of the time	All of the time
I have felt cheerful and in good spirits.	○	○	○	○	○	○
I have felt calm and relaxed.	○	○	○	○	○	○
I have felt active and vigorous.	○	○	○	○	○	○
I woke up feeling fresh and rested.	○	○	○	○	○	○
My daily life has been filled with things that interest me.	○	○	○	○	○	○

Please respond to the following statements.

	Not at all true	Hardly true	Moderately true	Exactly true
I can always manage to solve difficult problems if I try hard enough.	○	○	○	○
If someone opposes me, I can find the means and ways to get what I want.	○	○	○	○
It is easy for me to stick to my aims and accomplish my goals.	○	○	○	○
I am confident that I could deal efficiently with unexpected events.	○	○	○	○

	Not at all true	Hardly true	Moderately true	Exactly true
Thanks to my resourcefulness, I know how to handle unforeseen situations.	◯	◯	◯	◯
I can solve most problems if I invest the necessary effort.	◯	◯	◯	◯
I can remain calm when facing difficulties because I can rely on my coping abilities.	◯	◯	◯	◯
When I am confronted with a problem, I can usually find several solutions.	◯	◯	◯	◯
If I am in trouble, I can usually think of a solution.	◯	◯	◯	◯
I can usually handle whatever comes my way.	◯	◯	◯	◯

Section 3: Health Literacy ✓

How often do you need to have someone help you when you read instructions, pamphlets or other written material from your doctor or pharmacy?

- ◯ Always
- ◯ Often
- ◯ Sometimes
- ◯ Occasionally
- ◯ Never

Hypothetical - Control

Please read the hypothetical information below and answer the questions that follow. You are asked to imagine as if the following information is true. Please answer how you would feel or react if you were in this situation, to the best of your ability.

You are at the doctor (GP) after you recently had a small surgery done to remove one of your moles.

The doctor has the test results and says: “We found a melanoma in situ. We removed it all, with at least 3mm of normal skin around the melanoma in situ. You can decide whether or not you want us to remove more normal skin from around the scar. And you can also decide whether you would like to book in for regular skin checks with me every 6 months, or whether you would like us to teach you how to check your skin yourself and only book in to see us if you're worried about another mole. I recommend any of these options as a reasonable choice, and I will organise which ever ones you prefer."

Hypothetical - Label 1

Please read the information below and answer the questions that follow. Please note that you will be asked to imagine as if the following information is true. Please answer how you would feel or react if you were in this situation, to the best of your ability.

You are at the doctor (GP) after you recently had a small surgery done to remove one of your moles.

The doctor has the test results and says: “We found a low risk melanocytic neoplasm. We removed it all, with at least 3mm of normal skin around the low risk melanocytic neoplasm. You can decide whether or not you want us to remove more normal skin from around the scar. And you can also decide whether you would like to book in for regular skin checks with me every 6 months, or whether you would like us to teach you how to check your skin yourself and only book in to see us if you're worried about another mole. I recommend any of these options as a reasonable choice, and I will organise which ever ones you prefer."

Hypothetical - Label 2

Please read the information below and answer the questions that follow. Please note that you will be asked to imagine as if the following information is true. Please answer how you would feel or react if you were in this situation, to the best of your ability.

You are at the doctor (GP) after you recently had a small surgery done to remove one of your moles.

The doctor has the test results and says: “We found a low-risk melanocytic neoplasm, in situ. We removed it all, with at least 3mm of normal skin around the low-risk melanocytic neoplasm, in situ. You can decide whether or not you want us to remove more normal skin from around the scar. And you can also decide whether you would like to book in for regular skin checks with me every 6 months, or whether you would like us to teach you how to check your skin yourself and only book in to see us if you're worried about another mole. I recommend any of these options as a reasonable choice, and I will organise which ever ones you prefer."

Section 5: Primary and Secondary Outcome Measures ✓

After learning of your pathology result, how anxious do you feel?

Not anxious at all										Extemely anxious
0	1	2	3	4	5	6	7	8	9	10

How anxious

After learning of your pathology result, what percentage risk do you think you have of developing an invasive melanoma in your lifetime?

Low risk										High risk
0	10	20	30	40	50	60	70	80	90	100

How anxious

After learning of your pathology result, what percentage risk do you think you have of dying from melanoma?

Low risk										High risk
0	10	20	30	40	50	60	70	80	90	100

How anxious

After learning of your pathology result, which of these surgery management options would you choose?

- ◯ No further surgery
- ◯ Further surgery to remove more skin around the scar (so that the distance from the margins to the melanoma in situ are greater than 5 mm)

Please tell us how you decided on that surgery management option. What were

the important factors that helped you decide? [This question is optional].

After making that surgery management choice, how anxious do you feel?

Not anxious at all										Extemely anxious
0	1	2	3	4	5	6	7	8	9	10

How anxious

After learning of your pathology result, which of these follow up management options would you choose?

- ◯ I do my own skin checks with help from my partner/friend/relative. I am taught how to examine my total body and am given a special imaging device that clips on my phone. I have access to videos and online support to help me do skin checks and to use the imaging device. I can take images of any moles that concern me and send these to a dermatologist. If they are also concerned, then I am booked into clinic with my doctor for a skin check.
- ◯ My doctor does my skin check at regular 6 monthly appointments

Please tell us how you decided on that follow up management option. What were the important factors that helped you decide? [This question is optional].

After making that follow up management choice, how anxious do you feel?

Not anxious at all										Extemely anxious
0	1	2	3	4	5	6	7	8	9	10

How anxious

Section 6: Debrief Statement ✓

You were a participant in this study which aimed to investigate how people would react to different information provision on diagnosis of a low-risk prostate lesion results by the label given to the prostate lesion.

During the study, you were asked to imagine a hypothetical scenario in which you or your partner are given a diagnosis result after having gone to a routine screening. You were then asked to complete a series of survey questions.

You were randomised to receive one of three different hypothetical scenarios.

These three diagnosis scenarios were:

1. Diagnosis of a melanoma in situ.
2. Diagnosis of a low-risk melanocytic neoplasm.
3. Diagnosis of a low-risk melanocytic neoplasm, in situ.

The purpose of this study was to examine the impact of these different labels/diagnoses on preferred management strategy and psychological outcomes such as worry and health seeking intentions.

It is important to remember that this study was entirely hypothetical (made up). The study team does not have access to any of your medical history.

If you have any further questions regarding the study, feel free to contact Prof Katy Bell (katy.bell@sydney.edu.au)

For more information on melanoma and skin checks, please visit the following websites:

Melanoma Institute Australia

Cancer Council - Melanoma

Section 7: Feedback ✓

Thank you for your participation in the survey. Your time and contribution is greatly appreciated. If you are interested in the results of the study, the results and a lay summary of the results will be published at the following permanent web page: Wiser Healthcare publications

Powered by Qualtrics

BMJ Open

Impact of alternative diagnostic labels for melanoma in-situ on management choices and psychological outcomes: protocol for an online randomised study.

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2024-089558.R1
Article Type:	Protocol
Date Submitted by the Author:	31-Oct-2024
Complete List of Authors:	Wu, Zhuohan; The University of Sydney, Sydney School of Public Health, Faculty of Medicine and Health Nickel, Brooke; University of Sydney, Sydney School of Public Health, Faculty of Medicine and Health; Wiser Healthcare Research Collaboration boroumand, farzaneh; The University of Sydney Elder, David; Hospital of the University of Pennsylvania, Department of Pathology and Laboratory Medicine Ferguson, Peter M.; Melanoma Institute Australia; Royal Prince Alfred Hospital and NSW Health Pathology, Tissue Pathology and Diagnostic Oncology Scolyer, Richard; The University of Sydney O'Brien, Blake; Sullivan Nicolaides Pathology, Surgical Pathology Barnhill, Raymond; Paris Sciences and Lettres Research University, Department of Translational Research Adamson, Adewole S.; Austin, Department of Internal Medicine; The University of Texas at Austin Dell Medical School, van Akkooi, Alexander C.J.; Melanoma Institute Australia Emery, Jon; University of Melbourne, General Practice and Primary Care Academic Centre Parker, Lisa; University of Sydney Low, Donald; Cancer Voices New South Wales Low, Cynthia; Cancer Voices New South Wales Davies, Elspeth; Patient Researcher, Cambridge Liu, Sherrie; Health Consumers New South Wales Lewis, Stacey; Health Consumers New South Wales Spongberg-Ross, Bella; Health Consumers New South Wales Bell, Katy; The University of Sydney; Wiser Healthcare Research Collaboration
Primary Subject Heading:	Oncology
Secondary Subject Heading:	Health policy, Dermatology
Keywords:	Dermatological tumours < DERMATOLOGY, Adverse events < THERAPEUTICS, Clinical Decision-Making, Surgical dermatology < DERMATOLOGY, Surgical pathology < PATHOLOGY, Patient-Centered Care

Impact of alternative diagnostic labels for melanoma in-situ on management choices and psychological outcomes: protocol for an online randomised study.

Zhuohan Wu[1], Brooke Nickel[1,2], Farzaneh Boroumand[1,3], David Elder[4], Peter Ferguson[5,6], Richard A. Scolyer[5,6,7,8], Blake O'Brien[9], Raymond Barnhill[10], Adewole S Adamson[11], Alexander C.J. van Akkooi[5,12], Jon Emery[13], Lisa Parker[7,8,14], Donald Low[15], Cynthia Low[15], Elspeth Davies[16], Sherrie Liu[17], Stacey Lewis[17], Bella Spongberg-Ross[17], Katy JL Bell[1,2]

[1]Sydney School of Public Health, Faculty of Medicine and Health, The University of Sydney, Sydney, Australia.

[2] Wiser Healthcare Research Collaboration, Sydney, NSW, Australia

[3] School of Mathematical and Physical Sciences, Macquarie University, NSW, Australia

[4] Department of Pathology and Laboratory Medicine, Hospital of the University of Pennsylvania, Philadelphia

[5] Melanoma Institute Australia, The University of Sydney, Sydney, NSW, Australia

[6] Tissue Pathology and Diagnostic Oncology, Royal Prince Alfred Hospital and NSW Health Pathology, Sydney, NSW, Australia

[7] Faculty of Medicine and Health, The University of Sydney, Sydney, NSW, Australia

[8] Charles Perkins Centre, The University of Sydney, Sydney, NSW, Australia

[9] Sullivan Nicolaides Pathology, Brisbane, QLD, Australia

[10] Department of Translational Research, Institut Curie, Paris Sciences and Lettres Research University, and Faculty of Medicine University of Paris Descartes, Paris, France

[11]Department of Internal Medicine (Division of Dermatology), The University of Texas at Austin Dell Medical School, Austin, TX 78701, USA

[12] Royal Prince Alfred Hospital, Department of Melanoma and Surgical Oncology,

[13] Centre for Cancer Research, University of Melbourne, Melbourne, VIC, Australia

[14]Department of Radiation Oncology, Royal North Shore Hospital, Sydney, Australia

[15] Cancer Voices New South Wales, NSW, Australia

[16] Patient Advocate, Cambridge, UK

[17] Health Consumers New South Wales, NSW, Australia

Corresponding Author and guarantor: Katy Bell katy.bell@sydney.edu.au

Abstract

Introduction

A diagnosis of melanoma in-situ presents negligible risk to a person's lifespan or physical wellbeing, but existing terminology makes it difficult for patients to distinguish these from higher risk invasive melanomas. This study aims to explore whether using an alternative label for melanoma in situ may influence patients' management choices and anxiety levels.

Methods and Analysis

This study is a between-subjects randomised online experiment, using hypothetical scenarios. Following consent, eligible participants will be randomised 1:1:1 to three labels: "melanoma in situ" (control), "low-risk melanocytic neoplasm" (intervention 1) and "low-risk melanocytic neoplasm, in situ" (intervention 2). The required sample size is 1668 people. The co-primary outcomes are (i) choice between no further surgery or further surgery to ensure clear histological margins greater than 0.5mm, and (ii) choice between patient initiated clinical follow up when needed (patient-led surveillance) and regular routinely scheduled clinical follow-up (clinician-led surveillance). Secondary outcomes include diagnosis anxiety, perceived risk of invasive melanoma and of dying from melanoma, and management choice anxiety (after surgery choice and follow-up choice). We will make pairwise comparisons across the three diagnostic label groups using regression models (univariable and multivariable).

Ethics and Dissemination

The study has been registered with the Australian New Zealand Clinical Trials Registry (ID 386943). Ethics approval has been received from The University of Sydney Human Research Ethics Committee (2024/HE000019). Results of the study will be published in a peer-reviewed medical journal and a plain language summary of the findings will be shared on the Wiser Healthcare publications page https://www.wiserhealthcare.org.au/category/publications/.

Strengths and Limitations of This Study

- The randomised design enables robust comparison of diagnostic labels on decision-making and psychological outcomes.
- The study has been co-designed with consumers and clinicians to ensure labels and evidence are relevant to end-users.
- The large online randomised study will be representative of adults in the Australian community.
- The hypothetical nature of the study means it cannot capture experiences of patients after an actual melanoma in situ diagnosis (or alternative label) diagnosis. However, the scenario is a realistic one that they may experience (given the high rate of melanoma in situ diagnosis in Australia)
- The study does not explore the potential for recalibration of diagnostic thresholds using existing labels, the impact of diagnostic label on clinician's

management decisions, and the impact of providing detailed risk information (and whether this may modify diagnostic label effects)[1]. These are important areas for future research.

INTRODUCTION

Melanoma incidence and mortality trajectories in Australia and other countries show a classic epidemiologic signature of overdiagnosis[2]: steeply increasing incidence curves coupled with flat mortality trends[3-7]. While aging populations may lead to a small real increase in melanoma incidence[8], much of the increase is likely overdiagnosis[3-7].[3-7]. This appears to be largely driven by increased diagnosis of melanoma in situ[3 5 9], which in Australia is now diagnosed over twice as frequently as invasive melanoma[10]. Similar findings have been found for melanoma in the US (diagnosed at least as frequently as invasive melanoma)[4] and Denmark (diagnosed over half as frequently as invasive melanoma)[11].

Multiple evidence lines indicate that melanoma in situ is a risk factor for invasive melanoma rather than an obligate precursor[4 10 12 13].[4 10 12 13]. Overdiagnosis is partly driven by lowering the diagnostic threshold over the years, such that the same lesion that was called benign in the past, would now be labeled melanoma in situ[13]. Concerns about litigation may also be driving a tendency to interpret melanocytic lesions as a more severe diagnosis[14] particularly in partial biopsies or where the lesion extends to the surgical margins. Harms stemming from melanoma overdiagnosis include physical, psychosocial, and economic dimensions[15]. Physical harms can include overtreatment, repeat skin biopsies[16], scarring[16], pain, infection, and/or functional impairment. Psychological harms include anxiety and fear[17 18], with many

patients perceiving they have a high risk of dying from melanoma, when their actual risk is much lower (and risk all-cause mortality is actually lower than the population average)[19]. These psychological harms can manifest as anxiety about being outdoors, fear of cancer recurrence, or guilt for past UV exposure causing melanoma[6]. Social harms include impacts of the diagnosis on loved ones, and on patients' social networks[16]. Economic harms include treatment costs for the immediate diagnosis, and for future long term clinical surveillance. These incur substantial financial costs to both the health system and patient (as out-of-pocket costs), as well as opportunity costs for both clinician time and patient time. There is also a possible denial of life insurance as the person is now identified as a cancer survivor by many insurance companies (3).

One possible solution is to consider a new label for melanoma in situ without the word "melanoma"[13]. This might help patients recognize the lower risk of this type of lesion[19], and help to reduce the potential psychological harm. It may also pave the way for the de-escalation of treatment [20] and surveillance[21-23]. Evidence from other cancer contexts, including thyroid[24], breast[25], and prostate[26] lesions, suggests that new diagnostic labels may beneficially impact psychological outcomes and management decisions[27]. We seek to build on these findings by investigating the potential impacts of new labels for melanoma in situ. To ensure relevance of our findings to end-users, we will test alternative labels for melanoma in situ that were chosen by our co-

Investigators representing clinicians, patients, and the public. Alternative label(s) need to be acceptable to both patients and clinicians, and convey the low, but not zero, risk of future invasive melanoma. This study aims to explore whether using an alternative diagnostic label to communicate a hypothetical melanoma in situ diagnosis influences management choice and level of anxiety among Australian adults.

METHODS AND ANALYSIS

Study design

An online randomised study of Australian community members will be run, with, participants randomised to receive one of three hypothetical scenarios about the diagnosis of a melanoma in situ. Each group will be presented with a different diagnostic label, and we will survey participants about their preferred choices of management for that diagnosis, their level of anxiety about that diagnosis and their level of anxiety about their management choices.

This study is a between-subjects randomised online experiment. Following consent, eligible participants will be randomised 1:1:1 to "melanoma in situ" (control), "low risk melanocytic neoplasm" (intervention label 1), and "low risk melanocytic neoplasm, in situ" (intervention label 2). The co-primary outcomes and secondary outcomes will be compared across randomised groups.

There will be an equal probability of being assigned to each of the 3 groups, and we expect approximately equal numbers per group. We will use Qualtrics survey

software to randomly allocate participants into groups, present the scenarios, survey questions and collect data on the outcomes[28]. Our participants flow diagram present a summary of the randomisation of participants into the allocated control and intervention arms (Figure 1).

Eligibility criteria

Participants will be eligible if they are: 40 years or older, understand written English, and reside in Australia. Participants will be excluded if they have a history of melanoma (invasive or in-situ).

Recruitment and data collection.

Participants will be recruited from the general Australian public through an independent social research company (Dynata), which has a panel of 600,000 participants whose demographic characteristics align closely with those of the national population. Dynata has a points system in which participants receive points after completing surveys. The points can then be used to redeem vouchers, cash, or other rewards. Stratified sampling will be used, with quotas in place for gender (50% male, 50% female or other), age (25% for each of: 40-29 years, 50-59 years, 60-69 years, 70 years or older, +/- 15% allowed for first three age groups and +/-30% for oldest age group)[29], education (50% high school or less, 50% more than high school, +/-15% allowed), and State or Territory of residence (quotas proportionate to

Australian population, +/-5% allowed: New South Wales 31.3%, Victoria 25.6%, Queensland 20.5%, South Australia 6.9%, Western Australia 10.9%, Tasmania 2.1%, Northern Territory 0.9%, and Australian Capital Territory 1.7% [30]).

Participants who agree to participate in the study will complete an online Qualtrics survey managed by the research team. Only eligible participants will proceed to the randomisation step. The survey will capture baseline data and characteristics of participants including socio-demographic details including their age, location, health literacy, and personal and family history of any cancer, and participant responses on outcome measures. The survey questions are presented in the Supplement.

All data will be collected via Qualtrics software and hosted on The University of Sydney secure server. Information will be de-identified and we will not be able to link the survey back to participants. The non-identifiable data will be downloaded for analysis and stored within The University of Sydney's Research Data Store.

Determination of alternative labels to be tested.

We undertook a targeted literature search in September 2023 by retrieving forward and backward citation searches of four key papers on the topic[6 13 27 31]. We used the automated tool 'Spider Cite'[32]) to identify records, and Covidence to screen title, abstract and full-texts[33]. Of 593 unique records retrieved, we screened the full text of 27, and included 7 papers describing 9 alternative labels (see Box 1).

Using short online questionnaires implemented in Qualtrics[28], we then ran three

rounds of surveys with the 9 international Clinician co-Investigators (with expertise in dermatopathology, dermatology, surgical oncology, primary care, and radiation oncology), and 6 Patient/Public co-Investigators (two with lived experience of a melanoma diagnosis and four without a history of melanoma) to determine choice of alternative labels. This resulted in the final choice of two alternative labels that we will test in the online survey: ***low-risk melanocytic neoplasm*** and ***low-risk melanocytic neoplasm, in situ***.

Interventions

Participants will be randomised using Qualtrics randomisation software to receive one of three hypothetical scenarios. They will not be blinded. In each scenario, the participant will be told that the results of their recent skin surgery indicates a particular diagnosis. Group 1 (the control group) will be told they have a ***melanoma in situ***. Group 2 will be told they have a ***low-risk melanocytic neoplasm***. Group 3 will be told they have a ***low-risk melanocytic neoplasm, in situ***. We will not provide further explanation of what low-risk means.

Primary and Secondary Outcomes

Primary and secondary outcomes are described in Table 1. The co-primary outcomes are (i) participant's choice of surgical management option: no further surgery vs further surgery (to achieve pathology margins greater than 5mm), and (ii) follow-up

management option: patient led surveillance (self-skin examination with patient-initiated clinic visits) vs clinician led surveillance (six monthly routinely scheduled clinic visits).

The first co-primary outcome on surgical management choice reflects recent retrospective analyses that have found that narrower margins are likely to be as safe as margins currently recommended in guidelines in small melanoma in situ[34]. Indeed very narrow histological clearance (≥1mm) appears to be safe for melanoma in situ of the trunk and limbs[35]. The new MPATH-Dx V2.0 melanocytic lesion classification scheme recommends that provided margins are not involved, clinicians may consider not re-excising class II lesions – which includes melanoma in-situ[36]. The second co-primary outcome on follow-up management choice centres around patient-led surveillance (also called patient-initiated follow-up) as an alternative model of follow-up for cancer survivors to routinely scheduled clinic appointments[37]. Among people diagnosed and treated for early stage melanoma, patient-led surveillance is being evaluated in the MEL-SELF randomized controlled trial. Here, this model of care includes: training in self-skin examination, digital technologies to record and take images of concerning lesions (using a mobile dermatoscope), online system for submitting images for remote review by a dermatologist, and advice on whether urgent clinical review may be needed (teledermatology)[38].

Secondary outcomes are: diagnosis anxiety, perceived lifetime risk of invasive melanoma, perceived lifetime risk of dying from melanoma, management choice

anxiety, and open-text explanation of management choices (free text input).

Sample size

We estimated a sample size of 1668 participants with 556 participants per group in the study, which would provide 80% power (1 - β) to detect a pairwise difference in the proportion of choosing no further surgery, and 89% power to detect a pairwise difference in the proportion in choosing patient-led surveillance as small as 10%. The assumptions are: 50% would choose no further surgery (most conservative assumption) and 35%[23] would choose patient-led surveillance in the control label condition, a 5% dropout rate, $\alpha = 0.05$, the normal approximation to the binomial distribution, and the standard formula for comparing proportions in independent equal-sized groups.

Analysis

The analysis will focus on assessing the impact of different diagnostic labels for melanoma in situ on participants' psychological responses and healthcare decisions. Data analysts will be blinded to intervention assignment. For both co-primary outcomes, we will compare the proportion chosen for each management option. For first four secondary outcomes, we will compare summary statistical measures (means or medians) across randomised groups. For the last outcome, we will use thematic framework methods of qualitative data.

The analysis will adhere to the intention-to-treat principle, and participant data will be analyzed according to their randomly assigned diagnostic label group, regardless of adherence to the study protocol. The number of participant responses included in each analysis will be presented for each outcome. We will summarize categorical data for the randomised groups using counts and percentages, and continuous data using the minimum and maximum, mean, and standard deviation (SD) or median and interquartile range (IQR).

Statistical analyses will be conducted within a superiority framework to make pairwise comparisons across the three diagnostic label groups. Binary outcomes will be analyzed using logistic regression. Continuous outcomes will be analyzed using linear regression. For the cancer worry outcome, we will compare changes in worry across randomised groups by including baseline scores as a covariate in the regression model. Effect estimates for all primary and secondary outcomes will be presented with associated 95% confidence intervals (CI). All hypothesis tests will be two-sided with a significance level (α) of 5%. The potential for participants' health literacy to act as an effect modifier of intervention effects will be explored.

We will estimate unadjusted and adjusted effects using the relevant regression model. These will include variables used in sampling strata: age, education, geographic

location (by state/territory). Prognostic factors will be measured through the baseline questionnaire, and include baseline anxiety levels, sun exposure behavior, prior diagnosis of melanoma, diagnosis of melanoma in a family member. The effects of participants' health literacy on intervention effects will also be explored as a potential confounder.

Planned start and end dates for the study

The anticipated date of first participant enrolment was 01 July 2024 and the anticipated date of last data collection completion was 01 August 2024 (see Australian New Zealand Clinical Trials Registry entry ID 386943)

Patient and public involvement

Two authors have lived experience of a melanoma diagnosis (one had MIS and one had a thin stage I invasive melanoma), and four authors are members of the public. Two authors are affiliated with Cancer Voices NSW, one author is a patient researcher from Cambridge UK, and three authors are affiliated with Health Consumers NSW.

Ethics and Dissemination

Ethics approval of this project was provided by the University of Sydney on 06 May 2024 (No. 2024/HE000019). The study is registered with the Australian New Zealand Clinical Trials Registry (ID 386943). Updates to the protocol will be uploaded to the registry and identified by version number.

As this study is an online randomised experiment which includes a hypothetical scenario, we do not anticipate significant adverse events because of the trial interventions or conduct. Participants are reminded at several points before and after the study as part of the participant information, consent and debrief processes that the nature of the study is hypothetical, that none of the information relates to their actual health or wellbeing, and that researchers do not have access to their actual medical histories or information. The debriefing content also includes links to relevant resources for participants who wish to find out more.

Data availability statement

The research team will have access to the final dataset. Access may be granted to other researchers on reasonable request. No contractual agreements limit the disclosure of data to other investigators. The findings of the study will be published in a peer-reviewed medical journal. A lay summary of the findings will be published via permanent link at the Wiser Healthcare publications page.

Contributors

ZW co-led drafting of the manuscript, led drafting of the study questionnaire and application to the Human Research Ethics Committee, and assisted with the targeted literature review (full text screening and data extraction). BN and KB conceptualized the research, provided methodological expertise. KB, who is the guarantor, led the targeted literature review and the Clinician and Consumer Investigator survey to decide the choice of alternative labels, and co-led drafting of the manuscript. FB

calculated the sample size. BN, FB DE, PF, RS, BO, RB, AAd, AAk, JE, LP, DL, CL, ED, SLi, SLe, BSR and KB revised the manuscript. All authors read, contributed to, and approved the final manuscript.

Funding

National Health and Medical Research Council of Australia (NHMRC) Centre for Research Excellence Grant (2021/GNT2006545)

Brooke Nickel: NHMRC Investigator Grant (2020/GNT1113532)

RAS: NHMRC Investigator Grant (2022/GNT2018514)

Katy Bell: NHMRC Investigator Grant (2019/GNT1174523)

Declaration of Interests

RAS has received fees for professional services from SkylineDx BV, IO Biotech ApS, MetaOptima Technology Inc., F. Hoffmann-La Roche Ltd, Evaxion, Provectus Biopharmaceuticals Australia, Qbiotics, Novartis, Merck Sharp & Dohme, NeraCare, AMGEN Inc., Bristol-Myers Squibb, Myriad Genetics, GlaxoSmithKline.

AvA received Advisory Board/Consultancy Honoraria from 4SC AG, Amgen, Bristol-Myers Squibb, Merck Serono-Pfizer, MSD-Merck, Neracare, Novartis, Pierre Fabre, Sanofi, Sirius Medical, SkylineDX and Research Grants from Amgen, Merck Serono-Pfizer, SkylineDX.

All other authors have no conflicts of interest to declare.

References:

1. Bullen J, Nickel B, McCaffery K, et al. Impact of the diagnostic label for a low-risk prostate lesion: protocol for two online factorial randomised experiments. BMJ Open 2024;14(8):e085947. doi: 10.1136/bmjopen-2024-085947 [published Online First: 20240809]

2. Welch HG, Kramer Barnett S, Black William C. Epidemiologic Signatures in Cancer. New England Journal of Medicine 2019;381(14):1378-86. doi: 10.1056/NEJMsr1905447

3. Glasziou PP, Jones MA, Pathirana T, et al. Estimating the magnitude of cancer overdiagnosis in Australia. Med J Aust 2020;212(4):163-68. doi: 10.5694/mja2.50455 [published Online First: 2019/12/21]

4. Welch HG, Mazer BL, Adamson AS. The Rapid Rise in Cutaneous Melanoma Diagnoses. N Engl J Med 2021;384(1):72-79. doi: 10.1056/NEJMsb2019760 [published Online First: 2021/01/07]

5. Adewole SA, Geetanjali N, Mark AJ, et al. Ecological study estimating melanoma overdiagnosis in the USA using the lifetime risk method. BMJ Evidence-Based Medicine 2024:bmjebm-2023-112460. doi: 10.1136/bmjebm-2023-112460

6. Adamson AS, Suarez EA, Welch HG. Estimating Overdiagnosis of Melanoma Using Trends Among Black and White Patients in the US. JAMA Dermatology 2022;158(4):426-31. doi: 10.1001/jamadermatol.2022.0139

7. Mille Falk B, Emma Grundtvig G, John Brandt B. Overdiagnosis in malignant melanoma: a scoping review. BMJ Evidence-Based Medicine 2024;29(1):17. doi: 10.1136/bmjebm-2023-112341

8. Long GV, Swetter SM, Menzies AM, et al. Cutaneous melanoma. The Lancet 2023;402(10400):485-502. doi: 10.1016/S0140-6736(23)00821-8

9. Whiteman DC, Olsen CM, MacGregor S, et al. The effect of screening on melanoma incidence and biopsy rates. Br J Dermatol 2022;187(4):515-22. doi: 10.1111/bjd.21649 [published Online First: 2022/05/10]

10. Olsen CM, Pandeya N, Rosenberg PS, et al. Incidence of in Situ vs Invasive Melanoma: Testing the "Obligate Precursor" Hypothesis. J Natl Cancer Inst 2022;114(10):1364-70. doi: 10.1093/jnci/djac138 [published Online First: 2022/09/01]

11. Nielsen JB, Kristiansen IS, Thapa S. Increasing melanoma incidence with unchanged mortality: more sunshine, better treatment, increased diagnostic activity, overdiagnosis or lowered diagnostic threshold? British Journal of Dermatology 2024:ljae175. doi: 10.1093/bjd/ljae175

12. Elder DE. Obligate and Potential Precursors of Melanoma. JNCI: Journal of the National Cancer Institute 2022;114(10):1320-22. doi: 10.1093/jnci/djac139

13. Semsarian CR, Ma T, Nickel B, et al. Do we need to rethink the diagnoses melanoma in situ and severely dysplastic naevus? British Journal of Dermatology 2022;186(6):1030-32. doi: 10.1111/bjd.21010

14. Titus LJ, Reisch LM, Tosteson ANA, et al. Malpractice Concerns, Defensive Medicine, and the Histopathology Diagnosis of Melanocytic Skin Lesions. Am J Clin Pathol 2018;150(4):338-45. doi: 10.1093/ajcp/aqy057 [published Online First: 2018/07/15]

15. Bell KJL, Nijsten T. Melanoma overdiagnosis: why it matters and what can be done about it. Br J Dermatol 2022;187(4):459-60. doi: 10.1111/bjd.21750 [published Online First: 2022/08/06]

16. Elspeth D. Informed by research, transformed by research. BMJ Evidence-Based Medicine 2024;29(1):62. doi: 10.1136/bmjebm-2023-112646

17. Bell KJL, Mehta Y, Turner RM, et al. Fear of new or recurrent melanoma after treatment for localised melanoma. Psycho-Oncology 2017;26(11):1784-91. doi: https://doi.org/10.1002/pon.4366

18. Mahama AN, Haller CN, Labrada J, et al. Lived Experiences and Fear of Cancer Recurrence Among Survivors of Localized Cutaneous Melanoma. JAMA Dermatol 2024;160(5):495-501. doi: 10.1001/jamadermatol.2023.6158 [published Online First: 2024/02/14]

19. Patel VR, Roberson ML, Pignone MP, et al. Risk of Mortality After a Diagnosis of Melanoma In Situ. JAMA Dermatology 2023;159(7):703-10. doi: 10.1001/jamadermatol.2023.1494

20. Zijlker LP, Eggermont AMM, van Akkooi ACJ. The end of wide local excision (WLE) margins for melanoma ? European Journal of Cancer 2023;178:82-87. doi: https://doi.org/10.1016/j.ejca.2022.10.028

21. Moncrieff MD, Bastiaannet E, Underwood B, et al. Follow-up Schedule for Patients With Sentinel Node–negative Cutaneous Melanoma (The MELFO Study): An International Phase III Randomized Clinical Trial. Annals of Surgery 2022;276(4):e208-e16.

22. Lim W-Y, Morton RL, Turner RM, et al. Patient Preferences for Follow-up After Recent Excision of a Localized Melanoma. JAMA Dermatology 2018;154(4):420-27. doi: 10.1001/jamadermatol.2018.0021

23. Drabarek D, Ackermann D, Medcalf E, et al. Acceptability of a Hypothetical Reduction in Routinely Scheduled Clinic Visits Among Patients With History of a Localized Melanoma (MEL-SELF): Pilot Randomized Clinical Trial. JMIR Dermatol 2023;6:e45865. doi: 10.2196/45865

24. Nickel B, Barratt A, McGeechan K, et al. Effect of a Change in Papillary Thyroid Cancer Terminology on Anxiety Levels and Treatment Preferences: A Randomized Crossover Trial. JAMA Otolaryngol Head Neck Surg 2018;144(10):867-74. doi: 10.1001/jamaoto.2018.1272 [published Online First: 2018/10/20]

25. McCaffery K, Nickel B, Moynihan R, et al. How different terminology for ductal carcinoma in situ impacts women's concern and treatment preferences: a

randomised comparison within a national community survey. BMJ Open 2015;5(11):e008094. doi: 10.1136/bmjopen-2015-008094

26. Berlin A, Ramotar M, Santiago AT, et al. The influence of the “cancer” label on perceptions and management decisions for low-grade prostate cancer. JNCI: Journal of the National Cancer Institute 2023;115(11):1364-73. doi: 10.1093/jnci/djad108

27. Nickel B, Moynihan R, Barratt A, et al. Renaming low risk conditions labelled as cancer. Bmj 2018;362:k3322. doi: 10.1136/bmj.k3322 [published Online First: 2018/08/14]

28. Qualtrics. Qualtrics 2024 [Available from: https://www.qualtrics.com/.

29. Australian Bureau of Statistics (ABS). Regional population by age and sex 2023 [Available from: https://www.abs.gov.au/statistics/people/population/regional-population-age-and-sex/latest-release accessed 15 October 2024.

30. Australian Bureau of Statistics (ABS). National, state and territory population 2023 [Available from: https://www.abs.gov.au/statistics/people/population/national-state-and-territory-population/dec-2023 accessed 15 October 2024.

31. Elmore JG, Barnhill RL, Elder DE, et al. Pathologists' diagnosis of invasive melanoma and melanocytic proliferations: observer accuracy and reproducibility study. BMJ 2017;357:j2813. doi: 10.1136/bmj.j2813 [published Online First: 20170628]

32. Clark J, Glasziou P, Del Mar C, et al. A full systematic review was completed in 2 weeks using automation tools: a case study. J Clin Epidemiol 2020;121:81-90. doi: 10.1016/j.jclinepi.2020.01.008 [published Online First: 20200128]

33. Veritas Health Innovation. Covidence systematic review software [Available from: www.covidence.org.

34. Sun C, Lim A, De'Ambrosis B, et al. Recurrence Rate of Small Melanoma In Situ on Low-Risk Sites Excised With 5-mm Excisional Margin. JAMA Dermatology 2024;160(8) doi: 10.1001/jamadermatol.2024.1878

35. Smith H, Hussain W. Is it time we changed the way we manage melanoma in situ of the trunk and limbs? British Journal of Dermatology 2023;188(5):685-87. doi: 10.1093/bjd/ljad031

36. Barnhill RL, Elder DE, Piepkorn MW, et al. Revision of the Melanocytic Pathology Assessment Tool and Hierarchy for Diagnosis Classification Schema for Melanocytic Lesions: A Consensus Statement. JAMA Netw Open 2023;6(1):e2250613. doi: 10.1001/jamanetworkopen.2022.50613 [published Online First: 20230103]

37. Dretzke J, Chaudri T, Balaji R, et al. A systematic review of the effectiveness of patient-initiated follow-up after cancer. Cancer Medicine 2023;12(18):19057-71. doi: https://doi.org/10.1002/cam4.6462

38. Ackermann DM, Dieng M, Medcalf E, et al. Assessing the Potential for Patient-led Surveillance After Treatment of Localized Melanoma (MEL-SELF): A Pilot

453 Randomized Clinical Trial. JAMA Dermatology 2022;158(1):33-42. doi:
454 10.1001/jamadermatol.2021.4704
455 39. Vuong K, Armstrong BK, Weiderpass E, et al. Development and External
456 Validation of a Melanoma Risk Prediction Model Based on Self-assessed Risk
457 Factors. JAMA Dermatology 2016;152(8):889-96. doi:
458 10.1001/jamadermatol.2016.0939
459 40. World Health Organization. Wellbeing measures in primary health care/the
460 DepCare Project: report on a WHO meeting: Stockholm, Sweden, 12–13 February
461 1998: World Health Organization. Regional Office for Europe, 1998.
462 41. Scherer LD, Zikmund-Fisher BJ. Eliciting medical maximizing-minimizing
463 preferences with a single question: development and validation of the MM1. Medical
464 Decision Making 2020;40(4):545-50.
465 42. Morris NS, MacLean CD, Chew LD, et al. The Single Item Literacy Screener:
466 evaluation of a brief instrument to identify limited reading ability. BMC family
467 practice 2006;7:1-7.
468 43. Schwarzer R, Jerusalem M. Generalized self-efficacy scale. J Weinman, S Wright,
469 & M Johnston, Measures in health psychology: A user's portfolio Causal and control
470 beliefs 1995;35:37.
471 44. Davey HM, Barratt AL, Butow PN, et al. A one-item question with a Likert or
472 Visual Analog Scale adequately measured current anxiety. Journal of clinical
473 epidemiology 2007;60(4):356-60.

474 45. Dillard AJ, Ferrer RA, Welch JD. Associations between narrative transportation,
475 risk perception and behaviour intentions following narrative messages about skin
476 cancer. Psychology & Health 2017;33(5):573-93. doi:
477 10.1080/08870446.2017.1380811

478

Box 1: Process to select alternative labels to melanoma in situ for testing

• In the first-round surveys Clinician and Patient/Public co-Investigators indicated their ranking the 7 labels identified in the targeted literature search, and 2 additional labels in order of preference. The potential alternative labels from the literature search were: Melanocytic neoplasm of low malignant potential (8,24,25), Melanocytic neoplasm, Atypical neoplasm" (25), Severe or High-Grade Melanocytic Dysplasia, Superficial Atypical Melanocytic Proliferation of Uncertain Malignant Significance (SAMPUS) (26–28), Melanocytic Tumor of Uncertain Malignant Potential (MELTUMP), Melanocytoma (28). The two additional labels suggested by the research team were: low-risk melanocytic neoplasm and low-risk melanocytic lesion.

• In the second round surveys, co-Investigators indicated their preferred ranking of the top three choices from round 1 and two new labels suggested in round 1: Low-risk melanocytic neoplasm, Low-risk melanocytic lesion, and Melanocytic neoplasm of low malignant potential, Melanocytic intraepithelial neoplasia, and In situ melanocytic neoplasm.

• In the third round surveys, co-Investigators indicated their preferred ranking of the top two choices from round 2, and three new labels suggested in round 2: In situ melanocytic neoplasm, Low-risk melanocytic neoplasm, In situ melanocytic neoplasm, low risk, low-risk melanocytic neoplasm, in-situ, and dysplastic naevus. The two highest ranked labels, chosen as the alternative labels to test in the online

experiment, were: "***low-risk melanocytic neoplasm***" and "***low-risk melanocytic neoplasm, in-situ***".

479

480 **Table 1. Participant characteristics and outcome measures.**

Variable	Measure
Participant Characteristics	
Melanoma risk	Melanoma risk prediction based self-assessed risk factors[39]
General mood and wellbeing.	WHO (Five) Well-Being Questionnaire.[40]
Medical minimiser/maximiser.	Single-Item Maximiser/Minimiser Elicitation Question (MM1).[41]
Health literacy.	Single Item Literacy Screener (SILS).[42]
Melanoma worry.	Direct choice between specified options, one choice possible.
Self-efficacy.	Generalized Self-Efficacy Scale (GSE).[43]
Primary Outcomes	
Co-primary outcomes are choices for two management decisions. 1. Choice of further surgery: • No further surgery • Further surgery to ensure margins >0.5mm from lesion on pathology 2. Choice of follow-up: • Patient led surveillance: self-monitoring with patient-initiated clinic visits as needed • Clinician led surveillance: six monthly routinely scheduled clinic visits	Direct choice between two management approaches for each co-primary outcome Choice of further surgery and choice of follow-up.
Secondary Outcomes	
Diagnosis anxiety (feelings)	Single-question Visual Analogue Scale (0-6).[44 45]
Experiential perceived risk (vulnerability)	Single-question Visual Analogue Scale (0-6).[45]
Perceived lifetime absolute risk of invasive melanoma	Single-question Visual Analogue Scale (0-100).[45]
Perceived lifetime comparative risk of invasive melanoma	Single-question Visual Analogue Scale (0-6).[45]

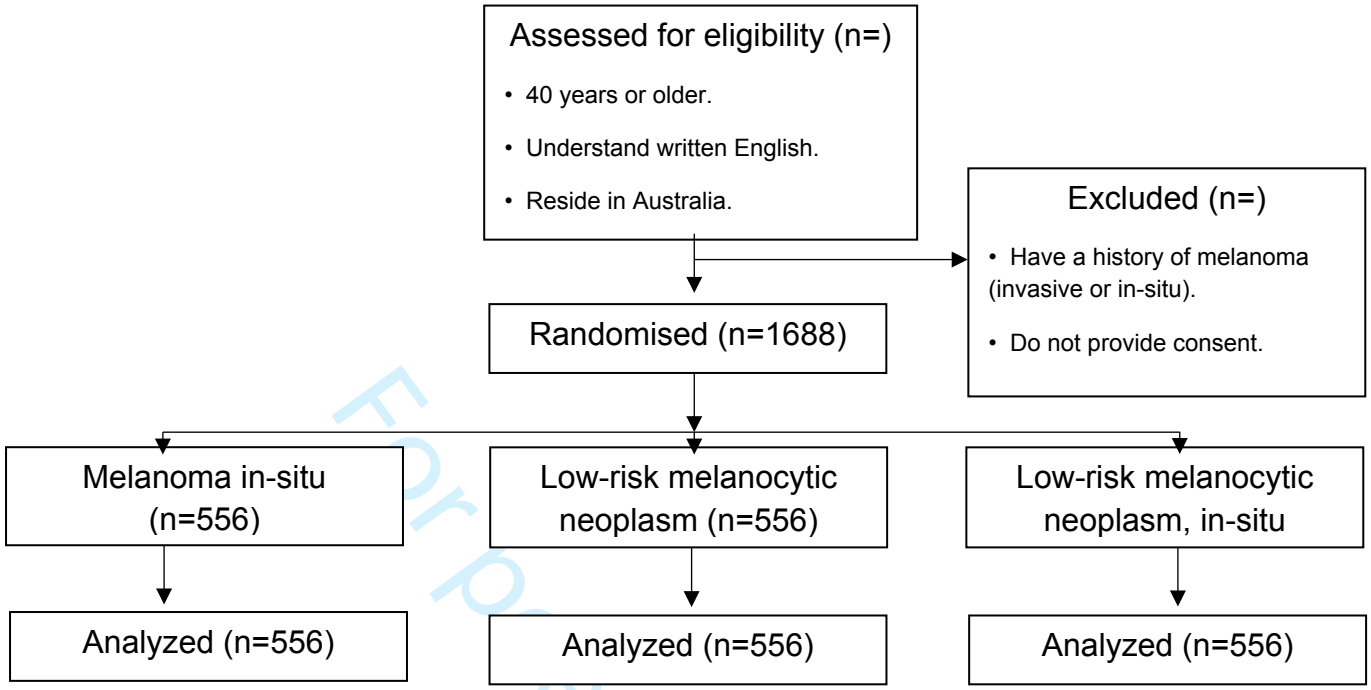
Perceived lifetime risk of dying from melanoma	Single-question Visual Analogue Scale (0-100).
Management choice anxiety.	Single-question Visual Analogue Scale (0-6).[44]
Open-text explanation of management choice.	Free text (optional)

481

482

Figure 1. Study Consolidated Standards of Reporting Trials flow diagram for participants. Participants' selection inclusion criteria are age over 40, understanding written English and residing in Australia. Patients will be excluded if they have melanoma, or do not provide consent.

Figure 1. Study CONSORT flow diagram



Landing Page ✓

Does the label for a low-risk melanocytic lesion influence management choice: a randomised experiment.

Thank you for your interest in our study about low-risk melanocytic lesions.

In this study, you will be randomised to be shown one of three hypothetical scenarios following surgery on a mole, which will be followed by questions about management options and anxiety.

The study is being conducted by a team of researchers from The University of Sydney School of Public Health. The team members are:

- Professor Katy Bell (School of Public Health at the University of Sydney)
- Dr Brooke Nickel (School of Public Health at the University of Sydney)
- Mr Zhuohan Wu (School of Public Health at the University of Sydney)

Taking part in the study involves completing one online questionnaire which will take approximately 10 minutes to complete.

Being in this study is completely voluntary and you do not have to take part. Your decision on whether to participate will not affect your current or future relationship with the researchers or anyone else at the University of Sydney.

Please take the time to read through the Participant Information Statement below.

If you are interested in taking part in this study, you will be asked to consent to take part by ticking the 'yes' box at the beginning of the questionnaire. By giving your consent to take part in this study, you are telling us that you:

✓ Understand what you have read in the Participant Information Statement.
✓ Agree to take part in the research study as outlined in Participant Information Statement.
✓ Agree to the use of your personal information as described.

When you have consented, you will fill out an online questionnaire that asks a series of questions, such as:

- Demographic questions, such as age, education, income level and relationship status.
- General health and cancer related questions.
- Melanoma and other cancer history related questions.

You will be randomised to read one of three **HYPOTHETICAL EXAMPLES** (these are made-up examples) in which different labels are used to explain a low-risk melanocytic skin lesion result. **Please note that you WILL NOT be receiving information or advice on any real mole check results or information about your actual health status**.

The hypothetical examples will be followed by questions about choice of management strategy and personal perspective.

Note that there is no back button. Please give your best answer to each question before moving on to the next.

Pre-Survey PIS ✓

You can click the link below to download the Participants Information Sheet for more information about this study.

Participants Information Sheet

Pre-Survey Consent Form ✓

Do you consent to take part in this study as described in the welcome page and Participants Information Sheet?

- ◯ Yes
- ◯ No

Section 1: Screening and Socio-Demographic ✓

Have you been previously diagnosed with a melanoma?

- ◯ Yes
- ◯ No

What is your age?

▾

Section 1.5: Screening and Socio-Demographic Part 2

Which of the following best describes your current gender identify?

- ◯ Male
- ◯ Female
- ◯ Non-binary / gender fluid
- ◯ Different identify

Which Australian state or territory do you currently live in?

- ◯ New South Wales
- ◯ Victoria
- ◯ Australian Capital Territory
- ◯ Queensland
- ◯ South Australia
- ◯ Western Australia
- ◯ Northern Territory
- ◯ Tasmania

Where are you located? (please enter your post code)

What is your highest level of education?

- ◯ Year 10 or below
- ◯ Year 11
- ◯ Year 12
- ◯ Certificate I/II
- ◯ Certficate III/IV
- ◯ Advanced diploma/diploma
- ◯ Bachelor's degree
- ◯ Graduate diploma/graduate certificate
- ◯ Postgraduate degree (Masters or Doctorate)

◯ Other - please specify:

What is your current employment status?

◯ Permanent or ongoing
◯ Fixed-term contract
◯ Casual/temporary (no paid sick leave or annual leave)
◯ Self-employed
◯ On paid leave (e.g. maternity leave)
◯ Unemployed
◯ Not working/not in the labour force (e.g. student, home duties, retired)

What was your total household income before taxes during the past 12 months?

◯ Less than AUD $30,000
◯ Between AUD $30,000 - $49,999
◯ Between AUD $50,000 - $79,999
◯ Between AUD $80,000 - $99,999
◯ Between AUD $100,000 - $149,999
◯ Between AUD $150,000 - $199,999
◯ AUD $200,000 or more
◯ Prefer not to say

Do you have private health insurance?

◯ Yes
◯ No
◯ Don't know

Do you have a partner?

- ◯ Spouse
- ◯ De-facto partner
- ◯ Partner who does not reside with you
- ◯ No partner
- ◯ Widowed
- ◯ Divorced or separated
- ◯ [ ] Other - please list:

Do you have children?

- ◯ Yes
- ◯ No
- ◯ Prefer not to say

Are you of Aboriginal or Torres Strait Islander origin?

- ◯ Aboriginal
- ◯ Torres Strait Islander
- ◯ Both Aboriginal and Torres Strait Islander
- ◯ Neither Aboriginal or Torres Strait Islander
- ◯ Prefer not to say

Were you born in Australia?

- ◯ Yes
- ◯ No

What is your country of birth?

- ◯ UK
- ◯ India
- ◯ China
- ◯ New Zealand
- ◯ The Philippines
- ◯ [ ] Other - please list:

In which year did you move to Australia?

[ ]

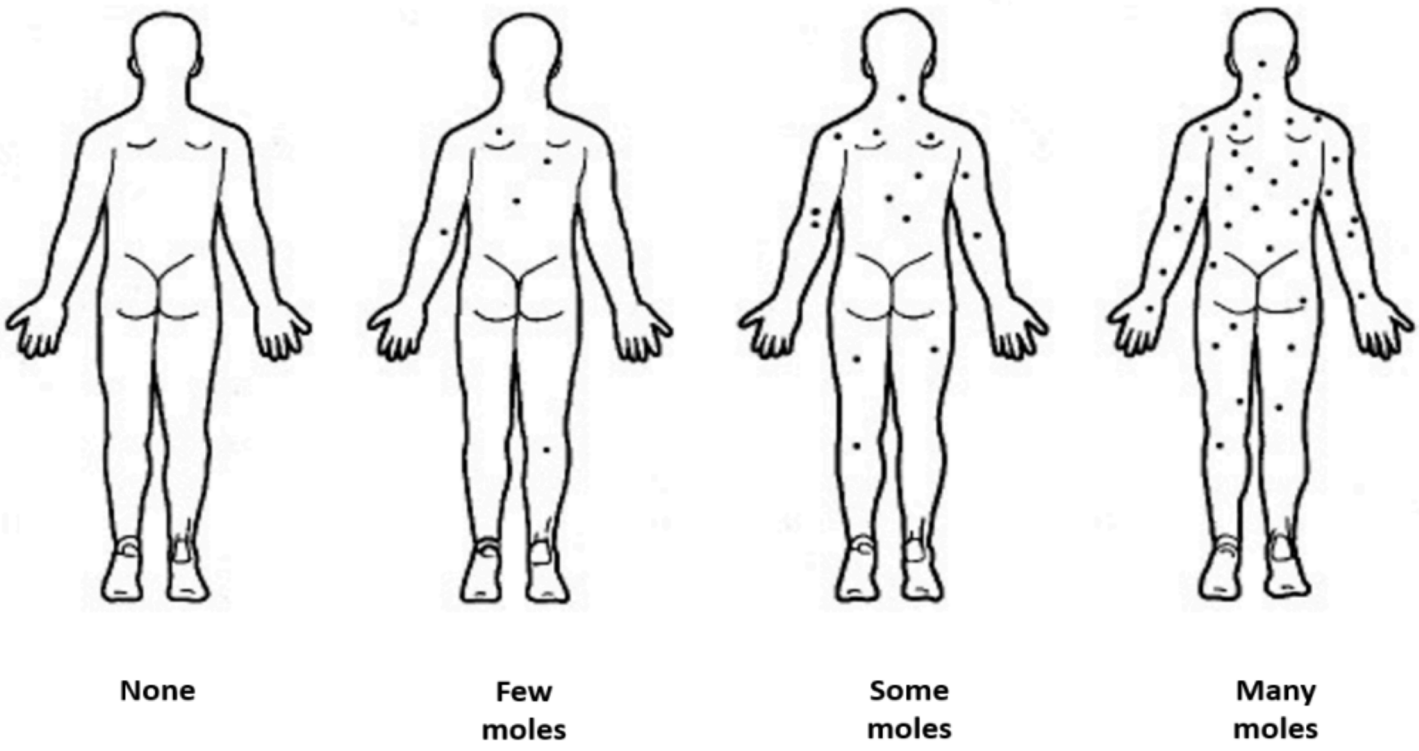
What language do you mostly speak at home?

- ◯ English
- ◯ Mandarin
- ◯ Arabic
- ◯ Cantonese
- ◯ Vietnamese
- ◯ [ ] Other - please list:

What was your natural hair colour when you were 18 years of age

- ◯ Black
- ◯ Brown
- ◯ Fair or Blond
- ◯ Red or Auburn

Looking at the image below, please select the option that approximately represents the number of moles on your body when you were aged 18 years, as best as you can remember.



- ◯ None
- ◯ Few moles
- ◯ Some moles
- ◯ Many moles

Have you ever used a sunbed or sunlamp?

- ◯ Yes
- ◯ No

Section 2: General Health Screening

Have you ever been diagnosed with any type of cancer?

- ◯ Yes
- ◯ No
- ◯ Don't know

Which type of cancer?

- ☐ Melanoma
- ☐ Skin (not melanoma)
- ☐ Prostate
- ☐ Breast
- ☐ Bowel
- ☐ Lung
- ☐ Lymphoma
- ☐ [ ] Other - please list:
- ☐ Don't know

Section 2: General Health ✓

In general, would you say your health is ...

- ◯ Excellent
- ◯ Very good
- ◯ Good
- ◯ Fair
- ◯ Poor

Has a current or former partner or a close friend ever been diagnosed with cancer?

- ◯ Yes

- ◯ No

Which type of cancer?

- ☐ Melanoma
- ☐ Skin (not melanoma)
- ☐ Prostate
- ☐ Breast
- ☐ Bowel
- ☐ Lung
- ☐ Lymphoma
- ☐ _____ Other - please list:
- ☐ Don't know

Has anyone in your close family ever been diagnosed with cancer?

- ◯ Yes
- ◯ No
- ◯ Don't know

Which type of cancer? Please tick all that apply

- ☐ Melanoma
- ☐ Skin (not melanoma)
- ☐ Prostate
- ☐ Breast
- ☐ Bowel
- ☐ Lung
- ☐ Lymphoma
- ☐ _____ Other - please list:

- [ ] Don't know

Who was this? Please tick all that apply

- ◯ Mother
- ◯ Father
- ◯ Sister
- ◯ Brother
- ◯ Daughter
- ◯ Son
- ◯ [ ] Other - please list:

How worried are you about developing melanoma?

- ◯ Not worried at all
- ◯ A bit worried
- ◯ Quite worried
- ◯ Very worried

Sometimes, medical action is clearly necessary and sometimes it is clearly not necessary.

Other times, reasonable people differ in their beliefs about whether medical action is needed.

In situations where it's not clear, do you tend to lean towards taking action or do you prefer to wait and see if action is needed?

Importantly, there is no right way to be.

- ◯ I strongly lean towards wait and see.

- ◯ I lean towards wait and see.
- ◯ I somewhat lean towards wait and see.
- ◯ I somewhat lean towards taking action.
- ◯ I lean towards taking action.
- ◯ I strongly lean towards taking action.

The following questions are related to how you have been feeling over the past two weeks. Please read each statement and then choose the most appropriate option regarding how you felt in the last two weeks.

	At no time	Some of the time	Less than half of the time	More than half of the time	Most of the time	All of the time
I have felt cheerful and in good spirits.	◯	◯	◯	◯	◯	◯
I have felt calm and relaxed.	◯	◯	◯	◯	◯	◯
I have felt active and vigorous.	◯	◯	◯	◯	◯	◯
I woke up feeling fresh and rested.	◯	◯	◯	◯	◯	◯
My daily life has been filled with things that interest me.	◯	◯	◯	◯	◯	◯

Please respond to the following statements.

	Not at all true	Hardly true	Moderately true	Mostly true
I can always manage to solve difficult problems if I try hard enough.	◯	◯	◯	◯
If someone opposes me, I can find the means and	◯	◯	◯	◯

	Not at all true	Hardly true	Moderately true	Mostly true
ways to get what I want.				
It is easy for me to stick to my aims and accomplish my goals.	◯	◯	◯	◯
I am confident that I could deal efficiently with unexpected events.	◯	◯	◯	◯
Thanks to my resourcefulness, I know how to handle unforeseen situations.	◯	◯	◯	◯

	Not at all true	Hardly true	Moderately true	Mostly true
I can solve most problems if I invest the necessary effort.	◯	◯	◯	◯
I can remain calm when facing difficulties because I can rely on my coping abilities.	◯	◯	◯	◯
When I am confronted with a problem, I can usually find several solutions.	◯	◯	◯	◯
If I am in trouble, I can usually think of a solution.	◯	◯	◯	◯
I can usually handle whatever comes my way.	◯	◯	◯	◯

Section 3: Health Literacy ✓

How often do you need to have someone help you when you read instructions, pamphlets or other written material from your doctor or pharmacy?

- ◯ Always
- ◯ Often
- ◯ Sometimes

◯ Occasionally

◯ Never

Randomized hypothetical labels

Please read the hypothetical information below and answer the questions that follow. You are asked to imagine as if the following information is true. Please answer how you would feel or react if you were in this situation, to the best of your ability.

You are at the doctor (GP) after you recently had a small surgery done to remove one of your moles.

The doctor has the pathology test results and says: “We found a **${e://Field/Label}**. We removed it all, and also 3mm of normal skin around the **${e://Field/Label}**."

Section 5: Primary and Secondary Outcome Measures ✓

Given the diagnosis of ${e://Field/Label}, how anxious do you feel?
Answer from Not at all anxious (0) to Extremely anxious(6).

	Not at all					Extremely
0	1	2	3	4	5	6

Given the diagnosis of ${e://Field/Label}, how vulnerable do you feel to developing invasive melanoma sometime in your life?
Answer from Not at all vulnerable (0) to Extremely vulnerable (6).

Not at all Extremely

0 1 2 3 4 5 6

Given the diagnosis of ${e://Field/Label}, on a scale of 0–100%, what do you think your chances are of **developing** an invasive melanoma sometime in your life?

Low risk (%) High risk (%)

0 10 20 30 40 50 60 70 80 90 100

Given the diagnosis of ${e://Field/Label}, what do you think your chances are of developing an invasive melanoma, compared to others of your age, gender, and skin colour?

Answer from Much lower chance (0) to Much higher chance (6).

Much lower Much higher

0 1 2 3 4 5 6

Given the diagnosis of ${e://Field/Label}, on a scale of 0 –100%, what do you think your chances are of **dying** from melanoma?

Low risk (%) High risk (%)

0 10 20 30 40 50 60 70 80 90 100

Please explain your reasoning behind the percentage you provided. [This question is optional]

Your doctor continues: "You now need to decide whether you would like us to do further surgery to remove more normal skin from around the scar, or whether you would prefer no further surgery at this time. I recommend either of these options as a reasonable choice and will organise whichever you prefer."

Given the diagnosis of ${e://Field/Label}, which of these surgery management options would you choose?

- ◯ Further surgery to remove more normal skin around the scar (so that the distance from the margins to the **${e://Field/Label}** is greater than 5 mm)
- ◯ No further surgery

Please tell us how you decided on that surgery management option. What were the important factors that helped you decide? [This question is optional].

After making that surgery management choice, how anxious do you feel?
Answer from Not at all anxious (0) to Extremely anxious (6).

Not at all						Extremely
0	1	2	3	4	5	6

Your doctor further explains that there are also different options for follow-up: "You need to also decide whether you would like to book in for regular skin checks with me every 6 months, or you would like us to teach you how to check your skin yourself (with tele-dermatologist support) and book in with me only if needed. Again, I recommend either option as a reasonable choice, and will organise whichever one you prefer."

Given the diagnosis of ${e://Field/Label}, which of these follow-up management options would you choose?

- ◯ My doctor does my skin check at regular 6 monthly appointments.
- ◯ I do my own skin checks with help from my partner/friend/relative (to check my back and other hard to see areas), and book in with my doctor when I need to.
  - I am taught how to examine my total body and am given a special imaging device that clips on my phone.
  - I have access to videos and online support to help me do skin checks and use the imaging device.
  - I can take images of any moles that concern me and send these to a dermatologist.
  - If the dermatologist is concerned, them I am booked in immediately for a skin check with my doctor.

Please tell us how you decided on that follow up management option. What were the important factors that helped you decide? [This question is optional].

After making that follow up management choice, how anxious do you feel?
Answer from Not at all anxious (0) to Extremely anxious (6).

Not at all						Extremely
0	1	2	3	4	5	6

Section 6: Debrief Statement ✓

You were a participant in this study which aimed to investigate how people would react to different information provision on diagnosis of a low-risk melanocytic lesion results by the label given to the melanocytic lesion.

During the study, you were asked to imagine a hypothetical scenario in which you are given a diagnosis result after having gone to a routine screening. You

were then asked to complete a series of survey questions.

You were randomised to receive one of three different hypothetical scenarios.

These three diagnosis scenarios were:

1. Diagnosis of a melanoma in situ.
2. Diagnosis of a low-risk melanocytic neoplasm.
3. Diagnosis of a low-risk melanocytic neoplasm, in situ.

The purpose of this study was to examine the impact of these different labels/diagnoses on preferred management strategy and psychological outcomes such as worry and health seeking intentions.

It is important to remember that this study was entirely hypothetical (made up). The study team does not have access to any of your medical history.

If you have any further questions regarding the study, feel free to contact Prof Katy Bell (katy.bell@sydney.edu.au)

For more information on melanoma and skin checks, please visit the following websites:

Melanoma Institute Australia
Cancer Council - Melanoma

We are conducting a follow-up study to explore individuals' experiences, concerns, and preferences regarding current and potential alternative labels for melanoma in situ. Would you be interested in participating in an interview

over the telephone or using web conferencing tools like Zoom or Microsoft Teams?

- ◯ Yes
- ◯ No

Thank you for your interest! Please provide your email address below so we can contact you to schedule the interview.

Section 7: Feedback ✓

Thank you for your participation in the survey. Your time and contribution is greatly appreciated. If you are interested in the results of the study, the results and a lay summary of the results will be published at the following permanent web page: Wiser Healthcare publications

BMJ Open

Impact of alternative diagnostic labels for melanoma in-situ on management choices and psychological outcomes: protocol for an online randomised study.

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2024-089558.R2
Article Type:	Protocol
Date Submitted by the Author:	18-Nov-2024
Complete List of Authors:	Wu, Zhuohan; The University of Sydney, Sydney School of Public Health, Faculty of Medicine and Health Nickel, Brooke; University of Sydney, Sydney School of Public Health, Faculty of Medicine and Health; Wiser Healthcare Research Collaboration boroumand, farzaneh; The University of Sydney Elder, David; Hospital of the University of Pennsylvania, Department of Pathology and Laboratory Medicine Ferguson, Peter M.; Melanoma Institute Australia; Royal Prince Alfred Hospital and NSW Health Pathology, Tissue Pathology and Diagnostic Oncology Scolyer, Richard; The University of Sydney O'Brien, Blake; Sullivan Nicolaides Pathology, Surgical Pathology Barnhill, Raymond; Paris Sciences and Lettres Research University, Department of Translational Research Adamson, Adewole S.; Austin, Department of Internal Medicine; The University of Texas at Austin Dell Medical School, van Akkooi, Alexander C.J.; Melanoma Institute Australia Emery, Jon; University of Melbourne, General Practice and Primary Care Academic Centre Parker, Lisa; University of Sydney Low, Donald; Cancer Voices New South Wales Low, Cynthia; Cancer Voices New South Wales Davies, Elspeth; Patient Researcher, Cambridge Liu, Sherrie; Health Consumers New South Wales Lewis, Stacey; Health Consumers New South Wales Spongberg-Ross, Bella; Health Consumers New South Wales Bell, Katy; The University of Sydney; Wiser Healthcare Research Collaboration
Primary Subject Heading:	Oncology
Secondary Subject Heading:	Health policy, Dermatology
Keywords:	Dermatological tumours < DERMATOLOGY, Adverse events < THERAPEUTICS, Clinical Decision-Making, Surgical dermatology < DERMATOLOGY, Surgical pathology < PATHOLOGY, Patient-Centered Care

Impact of alternative diagnostic labels for melanoma in-situ on management choices and psychological outcomes: protocol for an online randomised study.

Zhuohan Wu[1], Brooke Nickel[1,2], Farzaneh Boroumand[1,3], David Elder[4], Peter Ferguson[5,6], Richard A. Scolyer[5,6,7,8], Blake O'Brien[9], Raymond Barnhill[10], Adewole S Adamson[11], Alexander C.J. van Akkooi[5,12], Jon Emery[13], Lisa Parker[7,8,14], Donald Low[15], Cynthia Low[15], Elspeth Davies[16], Sherrie Liu[17], Stacey Lewis[17], Bella Spongberg-Ross[17], Katy JL Bell[1,2]

[1]Sydney School of Public Health, Faculty of Medicine and Health, The University of Sydney, Sydney, Australia.

[2] Wiser Healthcare Research Collaboration, Sydney, NSW, Australia

[3] School of Mathematical and Physical Sciences, Macquarie University, NSW, Australia

[4] Department of Pathology and Laboratory Medicine, Hospital of the University of Pennsylvania, Philadelphia

[5] Melanoma Institute Australia, The University of Sydney, Sydney, NSW, Australia

[6] Tissue Pathology and Diagnostic Oncology, Royal Prince Alfred Hospital and NSW Health Pathology, Sydney, NSW, Australia

[7] Faculty of Medicine and Health, The University of Sydney, Sydney, NSW, Australia

[8] Charles Perkins Centre, The University of Sydney, Sydney, NSW, Australia

[9] Sullivan Nicolaides Pathology, Brisbane, QLD, Australia

[10] Department of Translational Research, Institut Curie, Paris Sciences and Lettres Research University, and Faculty of Medicine University of Paris Descartes, Paris, France

[11]Department of Internal Medicine (Division of Dermatology), The University of Texas at Austin Dell Medical School, Austin, TX 78701, USA

[12] Royal Prince Alfred Hospital, Department of Melanoma and Surgical Oncology,

[13] Centre for Cancer Research, University of Melbourne, Melbourne, VIC, Australia

[14]Department of Radiation Oncology, Royal North Shore Hospital, Sydney, Australia

[15] Cancer Voices New South Wales, NSW, Australia

[16] Patient Advocate, Cambridge, UK

[17] Health Consumers New South Wales, NSW, Australia

Corresponding Author and guarantor: Katy Bell katy.bell@sydney.edu.au

Abstract

Introduction

A diagnosis of melanoma in-situ presents negligible risk to a person's lifespan or physical wellbeing, but existing terminology makes it difficult for patients to distinguish these from higher risk invasive melanomas. This study aims to explore whether using an alternative label for melanoma in situ may influence patients' management choices and anxiety levels.

Methods and Analysis

This study is a between-subjects randomised online experiment, using hypothetical scenarios. Following consent, eligible participants will be randomised 1:1:1 to three labels: "melanoma in situ" (control), "low-risk melanocytic neoplasm" (intervention 1) and "low-risk melanocytic neoplasm, in situ" (intervention 2). The required sample size is 1668 people. The co-primary outcomes are (i) choice between no further surgery or further surgery to ensure clear histological margins greater than 5 mm, and (ii) choice between patient initiated clinical follow up when needed (patient-led surveillance) and regular routinely scheduled clinical follow-up (clinician-led surveillance). Secondary outcomes include diagnosis anxiety, perceived risk of invasive melanoma and of dying from melanoma, and management choice anxiety (after surgery choice and follow-up choice). We will make pairwise comparisons across the three diagnostic label groups using regression models (univariable and multivariable).

Ethics and Dissemination

The study has been registered with the Australian New Zealand Clinical Trials Registry (ACTRN12624000740594). Ethics approval has been received from The University of Sydney Human Research Ethics Committee (2024/HE000019). Results of the study will be published in a peer-reviewed medical journal and a plain language summary of the findings will be shared on the Wiser Healthcare publications page https://www.wiserhealthcare.org.au/category/publications/.

Strengths and Limitations of This Study

- The randomised design enables robust comparison of diagnostic labels on decision-making and psychological outcomes.
- The study has been co-designed with patients, members of the public, and clinicians to ensure labels and evidence are relevant to end-users.
- The large online randomised study is representative of adults in the Australian community.
- The study's hypothetical nature limits its ability to capture real patients after an actual melanoma in situ diagnosis (or alternative label).
- The study does not explore the potential for recalibration of diagnostic thresholds using existing labels, the impact of diagnostic labels on actual patient or clinician decisions, or the impact of detailed risk information on diagnostic labels, all of which are areas for future research.

INTRODUCTION

Melanoma incidence and mortality trajectories in Australia and other countries show a classic epidemiologic signature of overdiagnosis[1]: steeply increasing incidence curves coupled with flat mortality trends[2-6]. While aging populations may lead to a small real increase in melanoma incidence[7], much of the increase is likely overdiagnosis[2-6]. This appears to be largely driven by increased diagnosis of melanoma in situ[2 4 8], which in Australia is now diagnosed over twice as frequently as invasive melanoma[9]. Similar findings have been found for melanoma in the US (diagnosed at least as frequently as invasive melanoma)[3] and Denmark (diagnosed over half as frequently as invasive melanoma)[10].

Multiple evidence lines indicate that melanoma in situ is a risk factor for invasive melanoma rather than an obligate precursor[3 9 11 12]. Overdiagnosis is partly driven by lowering the diagnostic threshold over the years, such that the same lesion that was called benign in the past, would now be labeled melanoma in situ[12]. Concerns about litigation may also be driving a tendency to interpret melanocytic lesions as a more severe diagnosis[13] particularly in partial biopsies or where the lesion extends to the surgical margins. Harms stemming from melanoma overdiagnosis include physical, psychosocial, and economic dimensions[14]. Physical harms can include overtreatment, repeat skin biopsies[15], scarring[15], pain, infection, and/or functional impairment. Psychological harms include anxiety and fear[16 17], with many patients perceiving they

have a high risk of dying from melanoma, when their actual risk is much lower (and risk all-cause mortality is actually lower than the population average)[18]. These psychological harms can manifest as anxiety about being outdoors, fear of cancer recurrence, or guilt for past UV exposure causing melanoma[5]. Social harms include impacts of the diagnosis on loved ones, and on patients' social networks[15]. Economic harms include treatment costs for the immediate diagnosis, and for future long term clinical surveillance. These incur substantial financial costs to both the health system and patient (as out-of-pocket costs), as well as opportunity costs for both clinician time and patient time. There is also a possible denial of life insurance as the person is now identified as a cancer survivor by many insurance companies[3].

One possible solution is to consider a new label for melanoma in situ without the word "melanoma"[12]. This might help patients recognize the lower risk of this type of lesion[18], and help to reduce the potential psychological harm. It may also pave the way for the de-escalation of treatment [19] and surveillance[20-22]. Evidence from other cancer contexts, including thyroid[23], breast[24], and prostate[25] lesions, suggests that new diagnostic labels may beneficially impact psychological outcomes and management decisions[26]. We seek to build on these findings by investigating the potential impacts of new labels for melanoma in situ. To ensure relevance of our findings to end-users, we will test alternative labels for melanoma in situ that were chosen by our co-Investigators representing clinicians, patients, and the public. Alternative label(s) need

to be acceptable to both patients and clinicians, and convey the low, but not zero, risk of future invasive melanoma. This study aims to explore whether using an alternative diagnostic label to communicate a hypothetical melanoma in situ diagnosis influences management choice and level of anxiety among Australian adults.

METHODS AND ANALYSIS

Study design

An online randomised study of Australian community members will be run, with, participants randomised to receive one of three hypothetical scenarios about the diagnosis of a melanoma in situ. Each group will be presented with a different diagnostic label, and we will survey participants about their preferred choices of management for that diagnosis, their level of anxiety about that diagnosis and their level of anxiety about their management choices.

This study is a between-subjects randomised online experiment. Following consent, eligible participants will be randomised 1:1:1 to “melanoma in situ” (control), “low risk melanocytic neoplasm” (intervention label 1), and “low risk melanocytic neoplasm, in situ” (intervention label 2). The co-primary outcomes and secondary outcomes will be compared across randomised groups.

There will be an equal probability of being assigned to each of the 3 groups, and we expect approximately equal numbers per group. We will use Qualtrics survey software to randomly allocate participants into groups, present the scenarios, survey

questions and collect data on the outcomes[27]. Our participants flow diagram present a summary of the randomisation of participants into the allocated control and intervention arms (Figure 1).

Eligibility criteria

Participants will be eligible if they are: 40 years or older, understand written English, and reside in Australia. Participants will be excluded if they have a history of melanoma (invasive or in-situ).

Recruitment and data collection.

Participants will be recruited from the general Australian public through an independent social research company (Dynata), which has a panel of 600,000 participants whose demographic characteristics align closely with those of the national population. Dynata has a points system in which participants receive points after completing surveys. The points can then be used to redeem vouchers, cash, or other rewards. Stratified sampling will be used, with quotas in place for gender (50% male, 50% female or other), age (25% for each of: 40-29 years, 50-59 years, 60-69 years, 70 years or older, +/- 15% allowed for first three age groups and +/-30% for oldest age group)[28], education (50% high school or less, 50% more than high school, +/-15% allowed), and State or Territory of residence (quotas proportionate to Australian population, +/-5% allowed: New South Wales 31.3%, Victoria 25.6%,

Queensland 20.5%, South Australia 6.9%, Western Australia 10.9%, Tasmania 2.1%, Northern Territory 0.9%, and Australian Capital Territory 1.7% [29]).

Participants who agree to participate in the study will complete an online Qualtrics survey managed by the research team. Only eligible participants will proceed to the randomisation step. The survey will capture baseline data and characteristics of participants including socio-demographic details including their age, location, health literacy, and personal and family history of any cancer, and participant responses on outcome measures. The survey questions are presented in the Supplement.

All data will be collected via Qualtrics software and hosted on The University of Sydney secure server. Information will be de-identified and we will not be able to link the survey back to participants. The non-identifiable data will be downloaded for analysis and stored within The University of Sydney's Research Data Store.

Determination of alternative labels to be tested.

We undertook a targeted literature search in September 2023 by retrieving forward and backward citation searches of four key papers on the topic[5 12 26 30]. We used the automated tool 'Spider Cite'[31]) to identify records, and Covidence to screen title, abstract and full-texts[32]. Of 593 unique records retrieved, we screened the full text of 27, and included 7 papers describing 9 alternative labels (see Box 1).

Using short online questionnaires implemented in Qualtrics[27], we then ran three rounds of surveys with the 9 international Clinician co-Investigators (with expertise in

dermatopathology, dermatology, surgical oncology, primary care, and radiation oncology), and 6 Patient/Public co-Investigators (two with lived experience of a melanoma diagnosis and four without a history of melanoma) to determine choice of alternative labels. This resulted in the final choice of two alternative labels that we will test in the online survey: ***low-risk melanocytic neoplasm*** and ***low-risk melanocytic neoplasm, in situ***.

Interventions

Participants will be randomised using Qualtrics randomisation software to receive one of three hypothetical scenarios. They will not be blinded. In each scenario, the participant will be told that the results of their recent skin surgery indicates a particular diagnosis. Group 1 (the control group) will be told they have a ***melanoma in situ***. Group 2 will be told they have a ***low-risk melanocytic neoplasm***. Group 3 will be told they have a ***low-risk melanocytic neoplasm, in situ***. We will not provide further explanation of what low-risk means.

Primary and Secondary Outcomes

Primary and secondary outcomes are described in Table 1. The co-primary outcomes are (i) participant's choice of surgical management option: no further surgery vs further surgery (to achieve pathology margins greater than 5 mm), and (ii) follow-up management option: patient led surveillance (self-skin examination with patient-

initiated clinic visits) vs clinician led surveillance (six monthly routinely scheduled clinic visits).

The first co-primary outcome on surgical management choice reflects recent retrospective analyses that have found that narrower margins are likely to be as safe as margins currently recommended in guidelines in small melanoma in situ[33]. Indeed very narrow histological clearance (≥1mm) appears to be safe for melanoma in situ of the trunk and limbs[34]. The new MPATH-Dx V2.0 melanocytic lesion classification scheme recommends that provided margins are not involved, clinicians may consider not re-excising class II lesions – which includes melanoma in-situ[35]. The second co-primary outcome on follow-up management choice centres around patient-led surveillance (also called patient-initiated follow-up) as an alternative model of follow-up for cancer survivors to routinely scheduled clinic appointments[36]. Among people diagnosed and treated for early stage melanoma, patient-led surveillance is being evaluated in the MEL-SELF randomized controlled trial. Here, this model of care includes: training in self-skin examination, digital technologies to record and take images of concerning lesions (using a mobile dermatoscope), online system for submitting images for remote review by a dermatologist, and advice on whether urgent clinical review may be needed (teledermatology)[37].

Secondary outcomes are: diagnosis anxiety, perceived lifetime risk of invasive melanoma, perceived lifetime risk of dying from melanoma, management choice anxiety, and open-text explanation of management choices (free text input).

Sample size

We estimated a sample size of 1668 participants with 556 participants per group in the study, which would provide 80% power (1 - β) to detect a pairwise difference in the proportion of choosing no further surgery, and 89% power to detect a pairwise difference in the proportion in choosing patient-led surveillance as small as 10%. The assumptions are: 50% would choose no further surgery (most conservative assumption) and 35%[22] would choose patient-led surveillance in the control label condition, a 5% dropout rate, $\alpha = 0.05$, the normal approximation to the binomial distribution, and the standard formula for comparing proportions in independent equal-sized groups.

Analysis

The analysis will focus on assessing the impact of different diagnostic labels for melanoma in situ on participants' psychological responses and healthcare decisions. Data analysts will be blinded to intervention assignment. For both co-primary outcomes, we will compare the proportion chosen for each management option. For first four secondary outcomes, we will compare summary statistical measures (means or medians) across randomised groups. For the last outcome, we will use thematic framework methods of qualitative data.

The analysis will adhere to the intention-to-treat principle, and participant data will be analyzed according to their randomly assigned diagnostic label group, regardless of adherence to the study protocol. The number of participant responses included in each analysis will be presented for each outcome. We will summarize categorical data for the randomised groups using counts and percentages, and continuous data using the minimum and maximum, mean, and standard deviation (SD) or median and interquartile range (IQR).

Statistical analyses will be conducted within a superiority framework to make pairwise comparisons across the three diagnostic label groups. Binary outcomes will be analyzed using logistic regression. Continuous outcomes will be analyzed using linear regression. For the cancer worry outcome, we will compare changes in worry across randomised groups by including baseline scores as a covariate in the regression model. Effect estimates for all primary and secondary outcomes will be presented with associated 95% confidence intervals (CI). All hypothesis tests will be two-sided with a significance level (α) of 5%. The potential for participants' health literacy to act as an effect modifier of intervention effects will be explored.

We will estimate unadjusted and adjusted effects using the relevant regression model. These will include variables used in sampling strata: age, education, geographic location (by state/territory). Prognostic factors will be measured through the baseline

questionnaire, and include baseline anxiety levels, sun exposure behavior, prior diagnosis of melanoma, diagnosis of melanoma in a family member. The effects of participants' health literacy on intervention effects will also be explored as a potential confounder.

Planned start and end dates for the study

The anticipated date of first participant enrolment was 01 July 2024 and the anticipated date of last data collection completion was 01 August 2024 (see Australian New Zealand Clinical Trials Registry, ID: ACTRN12624000740594)

Patient and public involvement

Two authors have lived experience of a melanoma diagnosis (one had MIS and one had a thin stage I invasive melanoma), and four authors are members of the public. Two authors are affiliated with Cancer Voices NSW, one author is a patient researcher from Cambridge UK, and three authors are affiliated with Health Consumers NSW.

Ethics and Dissemination

Ethics approval of this project was provided by the University of Sydney on 06 May 2024 (No. 2024/HE000019). The study is registered with the Australian New Zealand Clinical Trials Registry (ACTRN12624000740594). Updates to the protocol will be uploaded to the registry and identified by version number.

As this study is an online randomised experiment which includes a hypothetical

scenario, we do not anticipate significant adverse events because of the trial interventions or conduct. Participants are reminded at several points before and after the study as part of the participant information, consent and debrief processes that the nature of the study is hypothetical, that none of the information relates to their actual health or wellbeing, and that researchers do not have access to their actual medical histories or information. The debriefing content also includes links to relevant resources for participants who wish to find out more.

Data availability statement

The research team will have access to the final dataset. Access may be granted to other researchers on reasonable request. No contractual agreements limit the disclosure of data to other investigators. The findings of the study will be published in a peer-reviewed medical journal. A lay summary of the findings will be published via permanent link at the Wiser Healthcare publications page.

Contributors

ZW co-led drafting of the manuscript, led drafting of the study questionnaire and application to the Human Research Ethics Committee, and assisted with the targeted literature review (full text screening and data extraction). BN and KB conceptualized the research, provided methodological expertise. KB, who is the guarantor, led the targeted literature review and the Clinician and Consumer Investigator survey to decide the choice of alternative labels, and co-led drafting of the manuscript. FB calculated the sample size. BN, FB DE, PF, RS, BO, RB, AvA, AA, JE, LP, DL, CL,

ED, SLi, SLe, BSR and KB revised the manuscript. All authors read, contributed to, and approved the final manuscript.

Funding

National Health and Medical Research Council of Australia (NHMRC) Centre for Research Excellence Grant (2021/GNT2006545)

Brooke Nickel: NHMRC Investigator Grant (2020/GNT1113532)

RAS: NHMRC Investigator Grant (2022/GNT2018514)

Katy Bell: NHMRC Investigator Grant (2019/GNT1174523)

Declaration of Interests

RAS has received fees for professional services from SkylineDx BV, IO Biotech ApS, MetaOptima Technology Inc., F. Hoffmann-La Roche Ltd, Evaxion, Provectus Biopharmaceuticals Australia, Qbiotics, Novartis, Merck Sharp & Dohme, NeraCare, AMGEN Inc., Bristol-Myers Squibb, Myriad Genetics, GlaxoSmithKline.

AvA received Advisory Board/Consultancy Honoraria from 4SC AG, Amgen, Bristol-Myers Squibb, Merck Serono-Pfizer, MSD-Merck, Neracare, Novartis, Pierre Fabre, Sanofi, Sirius Medical, SkylineDX and Research Grants from Amgen, Merck Serono-Pfizer, SkylineDX.

All other authors have no conflicts of interest to declare.

References:

1. Welch HG, Kramer Barnett S, Black William C. Epidemiologic Signatures in Cancer. New England Journal of Medicine 2019;381(14):1378-86. doi: 10.1056/NEJMsr1905447

2. Glasziou PP, Jones MA, Pathirana T, et al. Estimating the magnitude of cancer overdiagnosis in Australia. Med J Aust 2020;212(4):163-68. doi: 10.5694/mja2.50455 [published Online First: 2019/12/21]

3. Welch HG, Mazer BL, Adamson AS. The Rapid Rise in Cutaneous Melanoma Diagnoses. N Engl J Med 2021;384(1):72-79. doi: 10.1056/NEJMsb2019760 [published Online First: 2021/01/07]

4. Adewole SA, Geetanjali N, Mark AJ, et al. Ecological study estimating melanoma overdiagnosis in the USA using the lifetime risk method. BMJ Evidence-Based Medicine 2024:bmjebm-2023-112460. doi: 10.1136/bmjebm-2023-112460

5. Adamson AS, Suarez EA, Welch HG. Estimating Overdiagnosis of Melanoma Using Trends Among Black and White Patients in the US. JAMA Dermatology 2022;158(4):426-31. doi: 10.1001/jamadermatol.2022.0139

6. Mille Falk B, Emma Grundtvig G, John Brandt B. Overdiagnosis in malignant melanoma: a scoping review. BMJ Evidence-Based Medicine 2024;29(1):17. doi: 10.1136/bmjebm-2023-112341

7. Long GV, Swetter SM, Menzies AM, et al. Cutaneous melanoma. The Lancet 2023;402(10400):485-502. doi: 10.1016/S0140-6736(23)00821-8

8. Whiteman DC, Olsen CM, MacGregor S, et al. The effect of screening on melanoma incidence and biopsy rates. Br J Dermatol 2022;187(4):515-22. doi: 10.1111/bjd.21649 [published Online First: 2022/05/10]

9. Olsen CM, Pandeya N, Rosenberg PS, et al. Incidence of in Situ vs Invasive Melanoma: Testing the "Obligate Precursor" Hypothesis. J Natl Cancer Inst 2022;114(10):1364-70. doi: 10.1093/jnci/djac138 [published Online First: 2022/09/01]

10. Nielsen JB, Kristiansen IS, Thapa S. Increasing melanoma incidence with unchanged mortality: more sunshine, better treatment, increased diagnostic activity, overdiagnosis or lowered diagnostic threshold? British Journal of Dermatology 2024:ljae175. doi: 10.1093/bjd/ljae175

11. Elder DE. Obligate and Potential Precursors of Melanoma. JNCI: Journal of the National Cancer Institute 2022;114(10):1320-22. doi: 10.1093/jnci/djac139

12. Semsarian CR, Ma T, Nickel B, et al. Do we need to rethink the diagnoses melanoma in situ and severely dysplastic naevus? British Journal of Dermatology 2022;186(6):1030-32. doi: 10.1111/bjd.21010

13. Titus LJ, Reisch LM, Tosteson ANA, et al. Malpractice Concerns, Defensive Medicine, and the Histopathology Diagnosis of Melanocytic Skin Lesions. Am J Clin Pathol 2018;150(4):338-45. doi: 10.1093/ajcp/aqy057 [published Online First: 2018/07/15]

14. Bell KJL, Nijsten T. Melanoma overdiagnosis: why it matters and what can be done about it. Br J Dermatol 2022;187(4):459-60. doi: 10.1111/bjd.21750 [published Online First: 2022/08/06]

15. Elspeth D. Informed by research, transformed by research. BMJ Evidence-Based Medicine 2024;29(1):62. doi: 10.1136/bmjebm-2023-112646

16. Bell KJL, Mehta Y, Turner RM, et al. Fear of new or recurrent melanoma after treatment for localised melanoma. Psycho-Oncology 2017;26(11):1784-91. doi: https://doi.org/10.1002/pon.4366

17. Mahama AN, Haller CN, Labrada J, et al. Lived Experiences and Fear of Cancer Recurrence Among Survivors of Localized Cutaneous Melanoma. JAMA Dermatol 2024;160(5):495-501. doi: 10.1001/jamadermatol.2023.6158 [published Online First: 2024/02/14]

18. Patel VR, Roberson ML, Pignone MP, et al. Risk of Mortality After a Diagnosis of Melanoma In Situ. JAMA Dermatology 2023;159(7):703-10. doi: 10.1001/jamadermatol.2023.1494

19. Zijlker LP, Eggermont AMM, van Akkooi ACJ. The end of wide local excision (WLE) margins for melanoma ? European Journal of Cancer 2023;178:82-87. doi: https://doi.org/10.1016/j.ejca.2022.10.028

20. Moncrieff MD, Bastiaannet E, Underwood B, et al. Follow-up Schedule for Patients With Sentinel Node–negative Cutaneous Melanoma (The MELFO Study):

An International Phase III Randomized Clinical Trial. Annals of Surgery 2022;276(4):e208-e16.

21. Lim W-Y, Morton RL, Turner RM, et al. Patient Preferences for Follow-up After Recent Excision of a Localized Melanoma. JAMA Dermatology 2018;154(4):420-27. doi: 10.1001/jamadermatol.2018.0021

22. Drabarek D, Ackermann D, Medcalf E, et al. Acceptability of a Hypothetical Reduction in Routinely Scheduled Clinic Visits Among Patients With History of a Localized Melanoma (MEL-SELF): Pilot Randomized Clinical Trial. JMIR Dermatol 2023;6:e45865. doi: 10.2196/45865

23. Nickel B, Barratt A, McGeechan K, et al. Effect of a Change in Papillary Thyroid Cancer Terminology on Anxiety Levels and Treatment Preferences: A Randomized Crossover Trial. JAMA Otolaryngol Head Neck Surg 2018;144(10):867-74. doi: 10.1001/jamaoto.2018.1272 [published Online First: 2018/10/20]

24. McCaffery K, Nickel B, Moynihan R, et al. How different terminology for ductal carcinoma in situ impacts women's concern and treatment preferences: a randomised comparison within a national community survey. BMJ Open 2015;5(11):e008094. doi: 10.1136/bmjopen-2015-008094

25. Berlin A, Ramotar M, Santiago AT, et al. The influence of the “cancer” label on perceptions and management decisions for low-grade prostate cancer. JNCI: Journal of the National Cancer Institute 2023;115(11):1364-73. doi: 10.1093/jnci/djad108

410 26. Nickel B, Moynihan R, Barratt A, et al. Renaming low risk conditions labelled as
411 cancer. Bmj 2018;362:k3322. doi: 10.1136/bmj.k3322 [published Online First:
412 2018/08/14]
413 27. Qualtrics. Qualtrics 2024 [Available from: https://www.qualtrics.com/.
414 28. Australian Bureau of Statistics (ABS). Regional population by age and sex 2023
415 [Available from: https://www.abs.gov.au/statistics/people/population/regional-
416 population-age-and-sex/latest-release accessed 15 October 2024.
417 29. Australian Bureau of Statistics (ABS). National, state and territory population
418 2023 [Available from: https://www.abs.gov.au/statistics/people/population/national-
419 state-and-territory-population/dec-2023 accessed 15 October 2024.
420 30. Elmore JG, Barnhill RL, Elder DE, et al. Pathologists' diagnosis of invasive
421 melanoma and melanocytic proliferations: observer accuracy and reproducibility
422 study. BMJ 2017;357:j2813. doi: 10.1136/bmj.j2813 [published Online First:
423 20170628]
424 31. Clark J, Glasziou P, Del Mar C, et al. A full systematic review was completed in 2
425 weeks using automation tools: a case study. J Clin Epidemiol 2020;121:81-90. doi:
426 10.1016/j.jclinepi.2020.01.008 [published Online First: 20200128]
427 32. Veritas Health Innovation. Covidence systematic review software [Available
428 from: www.covidence.org.

429 33. Sun C, Lim A, De'Ambrosis B, et al. Recurrence Rate of Small Melanoma In Situ
430 on Low-Risk Sites Excised With 5-mm Excisional Margin. JAMA Dermatology
431 2024;160(8) doi: 10.1001/jamadermatol.2024.1878
432 34. Smith H, Hussain W. Is it time we changed the way we manage melanoma in situ
433 of the trunk and limbs? British Journal of Dermatology 2023;188(5):685-87. doi:
434 10.1093/bjd/ljad031
435 35. Barnhill RL, Elder DE, Piepkorn MW, et al. Revision of the Melanocytic
436 Pathology Assessment Tool and Hierarchy for Diagnosis Classification Schema for
437 Melanocytic Lesions: A Consensus Statement. JAMA Netw Open
438 2023;6(1):e2250613. doi: 10.1001/jamanetworkopen.2022.50613 [published Online
439 First: 20230103]
440 36. Dretzke J, Chaudri T, Balaji R, et al. A systematic review of the effectiveness of
441 patient-initiated follow-up after cancer. Cancer Medicine 2023;12(18):19057-71. doi:
442 https://doi.org/10.1002/cam4.6462
443 37. Ackermann DM, Dieng M, Medcalf E, et al. Assessing the Potential for Patient-
444 led Surveillance After Treatment of Localized Melanoma (MEL-SELF): A Pilot
445 Randomized Clinical Trial. JAMA Dermatology 2022;158(1):33-42. doi:
446 10.1001/jamadermatol.2021.4704
447 38. Vuong K, Armstrong BK, Weiderpass E, et al. Development and External
448 Validation of a Melanoma Risk Prediction Model Based on Self-assessed Risk

Factors. JAMA Dermatology 2016;152(8):889-96. doi: 10.1001/jamadermatol.2016.0939

39. World Health Organization. Wellbeing measures in primary health care/the DepCare Project: report on a WHO meeting: Stockholm, Sweden, 12–13 February 1998: World Health Organization. Regional Office for Europe, 1998.

40. Scherer LD, Zikmund-Fisher BJ. Eliciting medical maximizing-minimizing preferences with a single question: development and validation of the MM1. Medical Decision Making 2020;40(4):545-50.

41. Morris NS, MacLean CD, Chew LD, et al. The Single Item Literacy Screener: evaluation of a brief instrument to identify limited reading ability. BMC family practice 2006;7:1-7.

42. Schwarzer R, Jerusalem M. Generalized self-efficacy scale. J Weinman, S Wright, & M Johnston, Measures in health psychology: A user's portfolio Causal and control beliefs 1995;35:37.

43. Davey HM, Barratt AL, Butow PN, et al. A one-item question with a Likert or Visual Analog Scale adequately measured current anxiety. Journal of clinical epidemiology 2007;60(4):356-60.

44. Dillard AJ, Ferrer RA, Welch JD. Associations between narrative transportation, risk perception and behaviour intentions following narrative messages about skin cancer. Psychology & Health 2017;33(5):573-93. doi: 10.1080/08870446.2017.1380811

470

Box 1: Process to select alternative labels to melanoma in situ for testing

• In the first-round surveys Clinician and Patient/Public co-Investigators indicated their ranking the 7 labels identified in the targeted literature search, and 2 additional labels in order of preference. The potential alternative labels from the literature search were: Melanocytic neoplasm of low malignant potential (8,24,25), Melanocytic neoplasm, Atypical neoplasm" (25), Severe or High-Grade Melanocytic Dysplasia, Superficial Atypical Melanocytic Proliferation of Uncertain Malignant Significance (SAMPUS) (26–28), Melanocytic Tumor of Uncertain Malignant Potential (MELTUMP), Melanocytoma (28). The two additional labels suggested by the research team were: low-risk melanocytic neoplasm and low-risk melanocytic lesion.

• In the second round surveys, co-Investigators indicated their preferred ranking of the top three choices from round 1 and two new labels suggested in round 1: Low-risk melanocytic neoplasm, Low-risk melanocytic lesion, and Melanocytic neoplasm of low malignant potential, Melanocytic intraepithelial neoplasia, and In situ melanocytic neoplasm.

• In the third round surveys, co-Investigators indicated their preferred ranking of the top two choices from round 2, and three new labels suggested in round 2: In situ melanocytic neoplasm, Low-risk melanocytic neoplasm, In situ melanocytic neoplasm, low risk, low-risk melanocytic neoplasm, in-situ, and dysplastic naevus.

The two highest ranked labels, chosen as the alternative labels to test in the online experiment, were: "***low-risk melanocytic neoplasm***" and "***low-risk melanocytic neoplasm, in-situ***".

471

472 **Table 1. Participant characteristics and outcome measures.**

Variable	Measure
Participant Characteristics	
Melanoma risk	Melanoma risk prediction based self-assessed risk factors[38]
General mood and wellbeing.	WHO (Five) Well-Being Questionnaire.[39]
Medical minimiser/maximiser.	Single-Item Maximiser/Minimiser Elicitation Question (MM1).[40]
Health literacy.	Single Item Literacy Screener (SILS).[41]
Melanoma worry.	Direct choice between specified options, one choice possible.
Self-efficacy.	Generalized Self-Efficacy Scale (GSE).[42]
Primary Outcomes	
Co-primary outcomes are choices for two management decisions. 1. Choice of further surgery: • No further surgery • Further surgery to ensure margins >5 mm from lesion on pathology 2. Choice of follow-up: • Patient led surveillance: self-monitoring with patient-initiated clinic visits as needed • Clinician led surveillance: six monthly routinely scheduled clinic visits	Direct choice between two management approaches for each co-primary outcome Choice of further surgery and choice of follow-up.
Secondary Outcomes	
Diagnosis anxiety (feelings)	Single-question Visual Analogue Scale (0-6).[43 44]
Experiential perceived risk (vulnerability)	Single-question Visual Analogue Scale (0-6).[44]
Perceived lifetime absolute risk of invasive melanoma	Single-question Visual Analogue Scale (0-100).[44]
Perceived lifetime comparative risk of invasive melanoma	Single-question Visual Analogue Scale (0-6).[44]

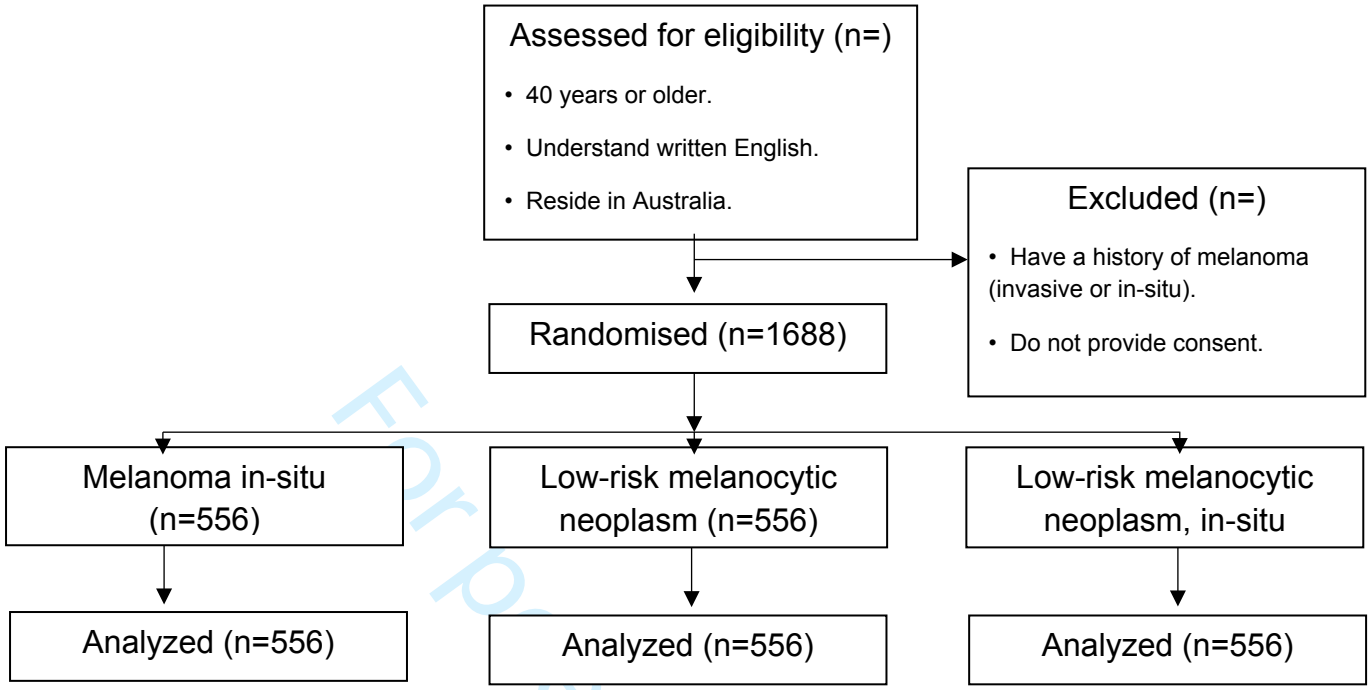
Perceived lifetime risk of dying from melanoma	Single-question Visual Analogue Scale (0-100).
Management choice anxiety.	Single-question Visual Analogue Scale (0-6).[43]
Open-text explanation of management choice.	Free text (optional)

473

474

Figure 1. Study Consolidated Standards of Reporting Trials flow diagram for participants. Participants' selection inclusion criteria are age over 40, understanding written English and residing in Australia. Patients will be excluded if they have melanoma, or do not provide consent.

Figure 1. Study CONSORT flow diagram



Landing Page ✓

Does the label for a low-risk melanocytic lesion influence management choice: a randomised experiment.

Thank you for your interest in our study about low-risk melanocytic lesions.

In this study, you will be randomised to be shown one of three hypothetical scenarios following surgery on a mole, which will be followed by questions about management options and anxiety.

The study is being conducted by a team of researchers from The University of Sydney School of Public Health. The team members are:

- Professor Katy Bell (School of Public Health at the University of Sydney)
- Dr Brooke Nickel (School of Public Health at the University of Sydney)
- Mr Zhuohan Wu (School of Public Health at the University of Sydney)

Taking part in the study involves completing one online questionnaire which will take approximately 10 minutes to complete.

Being in this study is completely voluntary and you do not have to take part. Your decision on whether to participate will not affect your current or future relationship with the researchers or anyone else at the University of Sydney.

Please take the time to read through the Participant Information Statement below.

If you are interested in taking part in this study, you will be asked to consent to take part by ticking the 'yes' box at the beginning of the questionnaire. By giving your consent to take part in this study, you are telling us that you:

✓ Understand what you have read in the Participant Information Statement.
✓ Agree to take part in the research study as outlined in Participant Information Statement.
✓ Agree to the use of your personal information as described.

When you have consented, you will fill out an online questionnaire that asks a series of questions, such as:

- Demographic questions, such as age, education, income level and relationship status.
- General health and cancer related questions.
- Melanoma and other cancer history related questions.

You will be randomised to read one of three **HYPOTHETICAL EXAMPLES** (these are made-up examples) in which different labels are used to explain a low-risk melanocytic skin lesion result. **Please note that you WILL NOT be receiving information or advice on any real mole check results or information about your actual health status**.

The hypothetical examples will be followed by questions about choice of management strategy and personal perspective.

Note that there is no back button. Please give your best answer to each question before moving on to the next.

Pre-Survey PIS ✓

You can click the link below to download the Participants Information Sheet for more information about this study.

Participants Information Sheet

Pre-Survey Consent Form ✓

Do you consent to take part in this study as described in the welcome page and Participants Information Sheet?

- ◯ Yes
- ◯ No

Section 1: Screening and Socio-Demographic ✓

Have you been previously diagnosed with a melanoma?

- ◯ Yes
- ◯ No

What is your age?

[ ]

Section 1.5: Screening and Socio-Demographic Part 2

Which of the following best describes your current gender identify?

- ◯ Male
- ◯ Female
- ◯ Non-binary / gender fluid
- ◯ Different identify

Which Australian state or territory do you currently live in?

- ◯ New South Wales
- ◯ Victoria
- ◯ Australian Capital Territory
- ◯ Queensland
- ◯ South Australia
- ◯ Western Australia
- ◯ Northern Territory
- ◯ Tasmania

Where are you located? (please enter your post code)

What is your highest level of education?

- ◯ Year 10 or below
- ◯ Year 11
- ◯ Year 12
- ◯ Certificate I/II
- ◯ Certficate III/IV
- ◯ Advanced diploma/diploma
- ◯ Bachelor's degree
- ◯ Graduate diploma/graduate certificate
- ◯ Postgraduate degree (Masters or Doctorate)

◯ Other - please specify:

What is your current employment status?

◯ Permanent or ongoing
◯ Fixed-term contract
◯ Casual/temporary (no paid sick leave or annual leave)
◯ Self-employed
◯ On paid leave (e.g. maternity leave)
◯ Unemployed
◯ Not working/not in the labour force (e.g. student, home duties, retired)

What was your total household income before taxes during the past 12 months?

◯ Less than AUD $30,000
◯ Between AUD $30,000 - $49,999
◯ Between AUD $50,000 - $79,999
◯ Between AUD $80,000 - $99,999
◯ Between AUD $100,000 - $149,999
◯ Between AUD $150,000 - $199,999
◯ AUD $200,000 or more
◯ Prefer not to say

Do you have private health insurance?

◯ Yes
◯ No
◯ Don't know

Do you have a partner?

- ◯ Spouse
- ◯ De-facto partner
- ◯ Partner who does not reside with you
- ◯ No partner
- ◯ Widowed
- ◯ Divorced or separated
- ◯ [ ] Other - please list:

Do you have children?

- ◯ Yes
- ◯ No
- ◯ Prefer not to say

Are you of Aboriginal or Torres Strait Islander origin?

- ◯ Aboriginal
- ◯ Torres Strait Islander
- ◯ Both Aboriginal and Torres Strait Islander
- ◯ Neither Aboriginal or Torres Strait Islander
- ◯ Prefer not to say

Were you born in Australia?

- ◯ Yes
- ◯ No

What is your country of birth?

- ◯ UK
- ◯ India
- ◯ China
- ◯ New Zealand
- ◯ The Philippines
- ◯ [ ] Other - please list:

In which year did you move to Australia?

[ ]

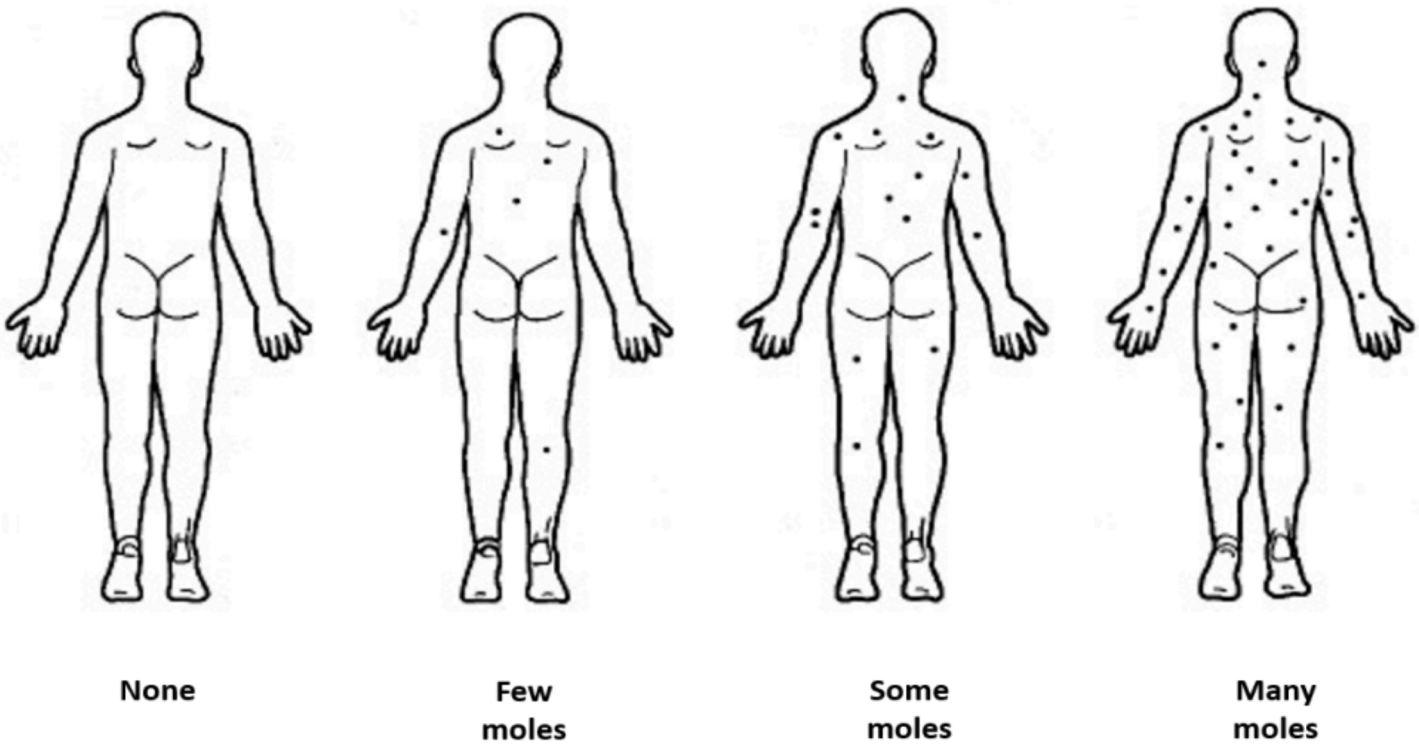
What language do you mostly speak at home?

- ◯ English
- ◯ Mandarin
- ◯ Arabic
- ◯ Cantonese
- ◯ Vietnamese
- ◯ [ ] Other - please list:

What was your natural hair colour when you were 18 years of age

- ◯ Black
- ◯ Brown
- ◯ Fair or Blond
- ◯ Red or Auburn

Looking at the image below, please select the option that approximately represents the number of moles on your body when you were aged 18 years, as best as you can remember.



- ◯ None
- ◯ Few moles
- ◯ Some moles
- ◯ Many moles

Have you ever used a sunbed or sunlamp?

- ◯ Yes
- ◯ No

Section 2: General Health Screening

Have you ever been diagnosed with any type of cancer?

- ◯ Yes
- ◯ No
- ◯ Don't know

Which type of cancer?

- ☐ Melanoma
- ☐ Skin (not melanoma)
- ☐ Prostate
- ☐ Breast
- ☐ Bowel
- ☐ Lung
- ☐ Lymphoma
- ☐ _____ Other - please list:
- ☐ Don't know

Section 2: General Health ✓

In general, would you say your health is ...

- ◯ Excellent
- ◯ Very good
- ◯ Good
- ◯ Fair
- ◯ Poor

Has a current or former partner or a close friend ever been diagnosed with cancer?

- ◯ Yes

- ◯ No

Which type of cancer?

- ☐ Melanoma
- ☐ Skin (not melanoma)
- ☐ Prostate
- ☐ Breast
- ☐ Bowel
- ☐ Lung
- ☐ Lymphoma
- ☐ _____ Other - please list:
- ☐ Don't know

Has anyone in your close family ever been diagnosed with cancer?

- ◯ Yes
- ◯ No
- ◯ Don't know

Which type of cancer? Please tick all that apply

- ☐ Melanoma
- ☐ Skin (not melanoma)
- ☐ Prostate
- ☐ Breast
- ☐ Bowel
- ☐ Lung
- ☐ Lymphoma
- ☐ _____ Other - please list:

☐ Don't know

Who was this? Please tick all that apply

- ◯ Mother
- ◯ Father
- ◯ Sister
- ◯ Brother
- ◯ Daughter
- ◯ Son
- ◯ [ ] Other - please list:

How worried are you about developing melanoma?

- ◯ Not worried at all
- ◯ A bit worried
- ◯ Quite worried
- ◯ Very worried

Sometimes, medical action is clearly necessary and sometimes it is clearly not necessary.

Other times, reasonable people differ in their beliefs about whether medical action is needed.

In situations where it's not clear, do you tend to lean towards taking action or do you prefer to wait and see if action is needed?

Importantly, there is no right way to be.

- ◯ I strongly lean towards wait and see.

- ◯ I lean towards wait and see.
- ◯ I somewhat lean towards wait and see.
- ◯ I somewhat lean towards taking action.
- ◯ I lean towards taking action.
- ◯ I strongly lean towards taking action.

The following questions are related to how you have been feeling over the past two weeks. Please read each statement and then choose the most appropriate option regarding how you felt in the last two weeks.

	At no time	Some of the time	Less than half of the time	More than half of the time	Most of the time	All of the time
I have felt cheerful and in good spirits.	◯	◯	◯	◯	◯	◯
I have felt calm and relaxed.	◯	◯	◯	◯	◯	◯
I have felt active and vigorous.	◯	◯	◯	◯	◯	◯
I woke up feeling fresh and rested.	◯	◯	◯	◯	◯	◯
My daily life has been filled with things that interest me.	◯	◯	◯	◯	◯	◯

Please respond to the following statements.

	Not at all true	Hardly true	Moderately true	Mostly true
I can always manage to solve difficult problems if I try hard enough.	◯	◯	◯	◯
If someone opposes me, I can find the means and	◯	◯	◯	◯

	Not at all true	Hardly true	Moderately true	Mostly true
ways to get what I want.				
It is easy for me to stick to my aims and accomplish my goals.	◯	◯	◯	◯
I am confident that I could deal efficiently with unexpected events.	◯	◯	◯	◯
Thanks to my resourcefulness, I know how to handle unforeseen situations.	◯	◯	◯	◯

	Not at all true	Hardly true	Moderately true	Mostly true
I can solve most problems if I invest the necessary effort.	◯	◯	◯	◯
I can remain calm when facing difficulties because I can rely on my coping abilities.	◯	◯	◯	◯
When I am confronted with a problem, I can usually find several solutions.	◯	◯	◯	◯
If I am in trouble, I can usually think of a solution.	◯	◯	◯	◯
I can usually handle whatever comes my way.	◯	◯	◯	◯

Section 3: Health Literacy ✓

How often do you need to have someone help you when you read instructions, pamphlets or other written material from your doctor or pharmacy?

- ◯ Always
- ◯ Often
- ◯ Sometimes

◯ Occasionally

◯ Never

Randomized hypothetical labels

Please read the hypothetical information below and answer the questions that follow. You are asked to imagine as if the following information is true. Please answer how you would feel or react if you were in this situation, to the best of your ability.

You are at the doctor (GP) after you recently had a small surgery done to remove one of your moles.

The doctor has the pathology test results and says: “We found a **${e://Field/Label}**. We removed it all, and also 3mm of normal skin around the **${e://Field/Label}**."

Section 5: Primary and Secondary Outcome Measures ✓

Given the diagnosis of ${e://Field/Label}, how anxious do you feel?
Answer from Not at all anxious (0) to Extremely anxious(6).

	Not at all					Extremely
0	1	2	3	4	5	6

Given the diagnosis of ${e://Field/Label}, how vulnerable do you feel to developing invasive melanoma sometime in your life?
Answer from Not at all vulnerable (0) to Extremely vulnerable (6).

Not at all Extremely

0 1 2 3 4 5 6

Given the diagnosis of ${e://Field/Label}, on a scale of 0–100%, what do you think your chances are of **developing** an invasive melanoma sometime in your life?

Low risk (%) High risk (%)

0 10 20 30 40 50 60 70 80 90 100

Given the diagnosis of ${e://Field/Label}, what do you think your chances are of developing an invasive melanoma, compared to others of your age, gender, and skin colour?

Answer from Much lower chance (0) to Much higher chance (6).

Much lower Much higher

0 1 2 3 4 5 6

Given the diagnosis of ${e://Field/Label}, on a scale of 0 –100%, what do you think your chances are of **dying** from melanoma?

Low risk (%) High risk (%)

0 10 20 30 40 50 60 70 80 90 100

Please explain your reasoning behind the percentage you provided. [This question is optional]

Your doctor continues: "You now need to decide whether you would like us to do further surgery to remove more normal skin from around the scar, or whether you would prefer no further surgery at this time. I recommend either of these options as a reasonable choice and will organise whichever you prefer."

Given the diagnosis of ${e://Field/Label}, which of these surgery management options would you choose?

- ◯ Further surgery to remove more normal skin around the scar (so that the distance from the margins to the **${e://Field/Label}** is greater than 5 mm)
- ◯ No further surgery

Please tell us how you decided on that surgery management option. What were the important factors that helped you decide? [This question is optional].

After making that surgery management choice, how anxious do you feel?
Answer from Not at all anxious (0) to Extremely anxious (6).

Not at all						Extremely
0	1	2	3	4	5	6

Your doctor further explains that there are also different options for follow-up: "You need to also decide whether you would like to book in for regular skin checks with me every 6 months, or you would like us to teach you how to check your skin yourself (with tele-dermatologist support) and book in with me only if needed. Again, I recommend either option as a reasonable choice, and will organise whichever one you prefer."

Given the diagnosis of ${e://Field/Label}, which of these follow-up management options would you choose?

- ◯ My doctor does my skin check at regular 6 monthly appointments.
- ◯ I do my own skin checks with help from my partner/friend/relative (to check my back and other hard to see areas), and book in with my doctor when I need to.
  - I am taught how to examine my total body and am given a special imaging device that clips on my phone.
  - I have access to videos and online support to help me do skin checks and use the imaging device.
  - I can take images of any moles that concern me and send these to a dermatologist.
  - If the dermatologist is concerned, them I am booked in immediately for a skin check with my doctor.

Please tell us how you decided on that follow up management option. What were the important factors that helped you decide? [This question is optional].

After making that follow up management choice, how anxious do you feel?
Answer from Not at all anxious (0) to Extremely anxious (6).

Not at all						Extremely
0	1	2	3	4	5	6

Section 6: Debrief Statement ✓

You were a participant in this study which aimed to investigate how people would react to different information provision on diagnosis of a low-risk melanocytic lesion results by the label given to the melanocytic lesion.

During the study, you were asked to imagine a hypothetical scenario in which you are given a diagnosis result after having gone to a routine screening. You

were then asked to complete a series of survey questions.

You were randomised to receive one of three different hypothetical scenarios.

These three diagnosis scenarios were:

1. Diagnosis of a melanoma in situ.
2. Diagnosis of a low-risk melanocytic neoplasm.
3. Diagnosis of a low-risk melanocytic neoplasm, in situ.

The purpose of this study was to examine the impact of these different labels/diagnoses on preferred management strategy and psychological outcomes such as worry and health seeking intentions.

It is important to remember that this study was entirely hypothetical (made up). The study team does not have access to any of your medical history.

If you have any further questions regarding the study, feel free to contact Prof Katy Bell (katy.bell@sydney.edu.au)

For more information on melanoma and skin checks, please visit the following websites:

Melanoma Institute Australia
Cancer Council - Melanoma

We are conducting a follow-up study to explore individuals' experiences, concerns, and preferences regarding current and potential alternative labels for melanoma in situ. Would you be interested in participating in an interview

over the telephone or using web conferencing tools like Zoom or Microsoft Teams?

- ◯ Yes
- ◯ No

Thank you for your interest! Please provide your email address below so we can contact you to schedule the interview.

Section 7: Feedback ✓

Thank you for your participation in the survey. Your time and contribution is greatly appreciated. If you are interested in the results of the study, the results and a lay summary of the results will be published at the following permanent web page: Wiser Healthcare publications