Accuracy of mobile digital teledermoscopy for skin self-examinations in adults at high risk of skin cancer: an open-label, randomised controlled trial

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Summary

Background Skin self-examinations supplemented with mobile teledermoscopy might improve early detection of skin cancers compared with naked-eye skin self-examinations. We aimed to assess whether mobile teledermoscopy-enhanced skin self-examination can improve sensitivity and specificity of self-detection of skin cancers when compared with naked-eye skin self-examination.

Methods This randomised, controlled trial was done in Brisbane (QLD, Australia). Eligible participants (aged ≥18 years) had at least two skin cancer risk factors as self-reported in the eligibility survey and had to own or have access to an iPhone compatible with a dermatoscope attachment (iPhone versions 5–8). Participants were randomly assigned (1:1), via a computer-generated randomisation procedure, to the intervention group (mobile dermoscopy-enhanced self-skin examination) or the control group (naked-eye skin self-examination). Control group and intervention group participants received web-based instructions on how to complete a whole body skin self-examination. All participants completed skin examinations at baseline, 1 month, and 2 months; intervention group participants submitted photographs of suspicious lesions to a dermatologist for telediagnosis after each skin examination and control group participants noted lesions on a body chart that was sent to the research team after each skin examination. All participants had an in-person whole-body clinical skin examination within 3 months of their last skin self-examination. Primary outcomes were sensitivity and specificity of skin self-examination, patient selection of clinically atypical lesions suspicious for melanoma or keratinocyte skin cancers (body sites examined, number of lesions photographed, types of lesions, and lesions missed), and diagnostic concordance of telediagnosis versus in-person whole-body clinical skin examination diagnosis. All primary outcomes were analysed in the modified intention-to-treat population, which included all patients who had a clinical skin examination within 3 months of their last skin self-examination. This trial was registered with the Australian and New Zealand Clinical Trials Registry, ACTRN12616000989448.

Findings Between March 6, 2017, and June 7, 2018, 234 participants consented to enrol in the study, of whom 116 (50%) were assigned to the intervention group and 118 (50%) were assigned to the control group. 199 participants (98 participants in the intervention group and 101 participants in the control group) attended the clinical skin examination and thus were eligible for analyses. Participants in the intervention group submitted 615 lesions (median 6·0 per person; range 1–24) for telediagnosis and participants in the control group identified and recorded 673 lesions (median 6·0 per person; range 1–16). At the lesion level, sensitivity for lesions clinically suspicious for skin cancer was 75% (95% CI 63–84) in the intervention group and 88% (95% CI 80–91) in the control group (p=0·04). Specificity was 87% (95% CI 85–90) in the intervention group and 89% (95% CI 87–91) in the control group (p=0·42). At the individual level, the intervention group had a sensitivity of 87% (95% CI 76–99) compared with 97% (95% CI 91–100) in the control group (p=0·26), and a specificity of 95% (95% CI 90–100) compared with 96% (95% CI 91–100) in the control group. The overall diagnostic concordance between the telediagnosis and in-person clinical skin examination was 88%.

Interpretation The use of mobile teledermoscopy did not increase sensitivity for the detection of skin cancers compared with naked-eye skin self-examination; thus, further evidence is necessary for inclusion of skin self-examination technology for public health benefit.

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Introduction

In the UK, which has a population of 66 million people, an estimated 15 970 adults developed melanoma between 2014 and 2016,[1] and 2285 died from the disease in 2016.[2] A similar number of melanoma cases and deaths associated with the disease are observed in Australia[3] despite the

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Research in context

Evidence before this study

Naked-eye skin self-examination is recommended by many cancer agencies for the early detection of skin cancers. The use of dermoscopy has improved the sensitivity of dermatologists for diagnosing skin cancers, but it is unclear whether the use of dermoscopy during skin self-examination could also improve the sensitivity of lay people when assessing their own skin.
We searched PubMed for studies published between database inception and Sept 30, 2019, using the search terms "mobile teledermatology OR mobile teledermoscopy" AND "skin cancer OR melanoma". No previous randomised controlled trials were identified that directly compared naked-eye skin self-examination (as currently recommended by cancer agencies) with mobile teledermoscopy-enhanced skin self-examination.

Added value of this study

This is the first randomised trial to directly compare mobile teledermoscopy assisted skin self-examination with naked-eye skin self-examination to assess whether teledermoscopy improves the sensitivity and specificity of lay people for selecting lesions suspicious for skin cancer. Although previous studies have provided evidence for feasibility and acceptability of mobile teledermoscopy, accuracy outcomes were not directly compared with current best practice guidelines of naked-eye skin self-examination.

Implications of all the available evidence

In our study, the intervention and control groups achieved high sensitivity and similar specificity for the identification of lesions suspicious for skin cancer, but supplementing skin examination with mobile teledermoscopy did not improve sensitivity for skin cancer compared with naked-eye skin self-examination. For the early detection of skin cancer, naked-eye skin self-examination should continue to be recommended by cancer agencies.

country having a smaller population than the UK (around 25 million). The term skin cancer includes melanoma (a skin malignancy that stems from the melanocytes), keratinocyte cancers (basal cell carcinoma or squamous cell carcinoma), which are the most common types of skin cancer with more than 210 000 cases reported in 2015 in the UK,[4] and other less common types of skin cancer. In Australia, keratinocyte cancers are more common than any other cancer and it is estimated that more than 560 people die from these cancers each year.[5] Diagnosis of skin cancers at an earlier stage is strongly associated with better survival, lower morbidity, and reduced health-care costs.[6–8] Since health services are increasingly provided digitally using direct-to-consumer technologies,[9] further evidence is urgently needed to ascertain whether digital approaches can optimise early detection of skin cancer, especially in populations at high risk.

Most skin cancers, including melanoma, are initially detected by patients themselves or by their families.[10,11] In the absence of population-based screening programmes, cancer agencies recommend the practice of regular naked-eye skin self-examinations, whereby a person checks their own skin and consults a doctor if they notice any changes.[12,13] Previous studies that investigated the sensitivity of skin self-examination found that sensitivity varied widely from 25% to 93%;[14,15] had small sample sizes; used non-randomised trial designs; or asked participants to identify skin lesions that had been changed artificially.[15]

In the past decade, mobile teledermoscopy technologies have become available, offering the potential to improve skin self-examination. Mobile teledermoscopy-enhanced skin self-examination combines the photographic and telecommunication features of smartphones with a magnifying device that has a polarised light source. In combination with an app, this technology allows people to view, photograph, store, and send dermoscopic images of suspicious skin lesions to a medical provider. Theoretical advantages of mobile teledermoscopy include promoting a thorough skin self-examination and requiring close inspections of skin lesions for photographing. Previous studies have assessed the feasibility of mobile teledermoscopy, showing that people can use the imaging and transmission process to detect suspicious skin lesions.[16–20] However, none of these studies directly compared naked-eye skin self-examination with mobile teledermoscopy-enhanced skin self-examination in a randomised trial setting.

We aimed to assess whether mobile teledermoscopy-enhanced skin self-examination can improve sensitivity and specificity of self-detection of skin cancers when compared with naked-eye skin self-examination.

Methods

Study design and participants

This open-label, randomised controlled trial was done at The University of Queensland and The Queensland University of Technology (Brisbane, QLD, Australia). Participants were recruited through university email channels, television news, and social media. Eligible participants were aged 18 years or older; had at least two skin cancer risk factors as self-reported in the eligibility survey (light skin complexion and fair hair; skin that never or rarely tans, and always or mostly burns; a family history of melanoma or a personal history of skin cancer, or many naevi; and residing in Queensland). Eligible individuals also had to have access to an iPhone compatible with the dermatoscope attachment (iPhone versions 5–8); had to be willing to travel to The Queensland University of Technology for an in-person whole-body clinical skin examination; and had to have a partner to assess difficult-to-see body areas. Participants were excluded if they had a

history of melanoma within the past 5 years because such diagnoses would require frequent surveillance by a doctor.

The study was approved by the Queensland University of Technology Human Research Ethics Committee. The study protocol is provided in the appendix (p 2) and has been published previously.[21]

Randomisation and masking

Participants were randomly assigned (1:1) to the intervention group or control group using a computer-generated randomisation sequence. Randomisation was done by research staff using trial database software (REDCap; Vanderbilt University, Nashville, TN, USA). REDCap facilitates allocation concealment; therefore research staff were masked to the next sequence. Participants, research staff, and dermatologists were aware of group allocation. Analyses were done by a statistician masked to group allocation.

Procedures

Naked-eye skin self-examination is defined as an individual examining themselves for early skin cancer without use of examination aids with the exception of a mirror or help from a partner to inspect areas of the body that are difficult to see. Mobile teledermoscopy is defined as a store-and-forward system for sending images of skin lesions suspicious for skin cancer to a medical practitioner for diagnosis. Intervention group participants received the FotoFinder handyscope (FotoFinder Systems GmbH, Bad Birnbach, Germany; appendix (p 26) by mail and did mobile teledermoscopy-enhanced skin self-examination in their homes. Participants were provided with web-based instructions on how to complete a whole-body skin self-examination. To guide selection of lesions suspicious for melanoma, participants were provided with the asymmetry and colour rule and accompanying macro images of melanomas.[22] For lesions suspicious for other skin cancers, participants were provided with example macro images of basal cell carcinoma and squamous cell carcinoma and a description of their features. Intervention group participants additionally received examples of dermoscopic images of skin cancers. To allow the assessment of change, participants did skin self-examinations at 1 month and 2 months; participants were asked to rephotograph the same lesions from baseline and any new suspicious lesions that might have developed, and send all photographed lesions to the study team via the FotoFinder handyscope patient app (appendix p 26). A dermatologist (HPS) provided a telediagnosis for every submitted lesion. Participants were advised that they would receive the telediagnosis results at the in-person clinical skin examination, unless immediate action was required (ie, suspected melanoma, basal cell carcinoma, or squamous cell carcinoma). Participants who submitted photographs indicating that treatment or excision was required were contacted within 1 week and asked to visit their general practitioner promptly with a referral letter.

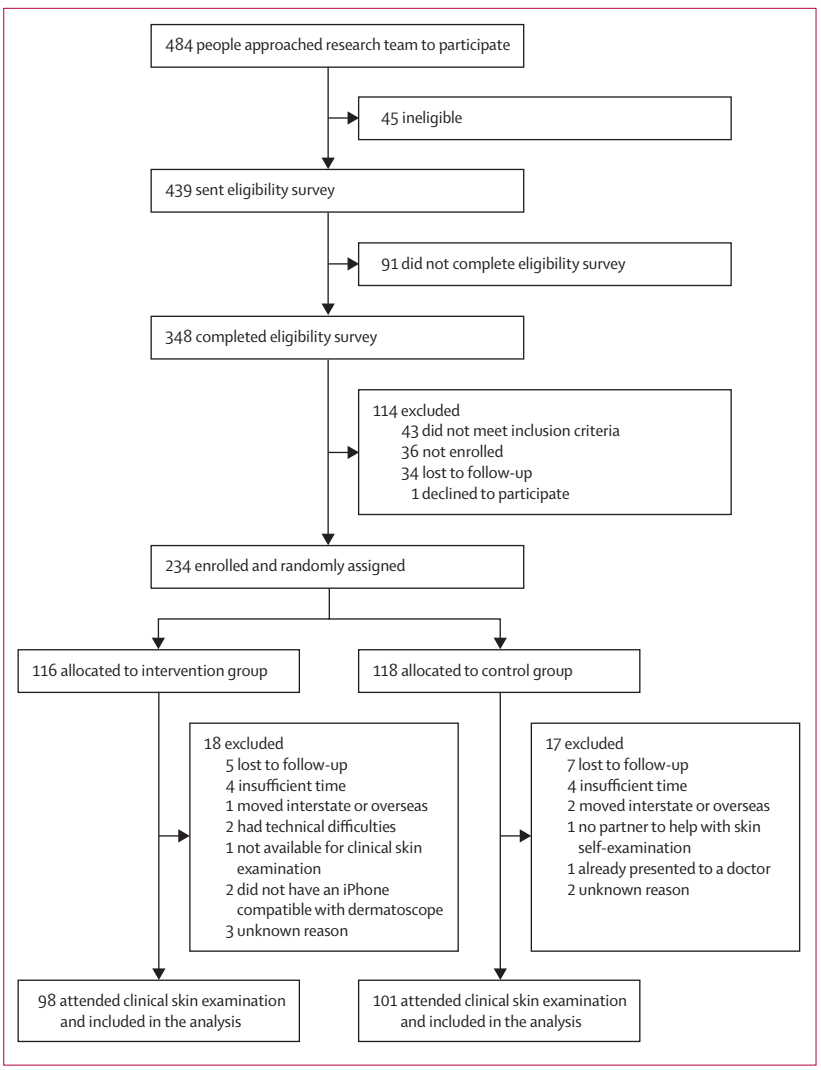

Figure: **Trial profile**

The first three teledermoscopic images submitted by a random sample of 30 participants (90 lesions) were diagnosed by two additional dermatologists (CC-L and RH-W) in addition to the study dermatologist (HPS). The diagnostic agreement between the three dermatologists was 99%.

Participants in the control group were asked to do a naked-eye skin self-examination at baseline, mark all lesions they were concerned about on a body chart, to check the same lesions again at 1 month and 2 months, and add any newly noted lesions. Control group participants received web-based instructions on how to complete a whole-body skin self-examination (the same instructions as the intervention group): the asymmetry and colour rule, and example macro images of melanoma, basal cell carcinoma, and squamous cell carcinoma. After every skin check, participants emailed a copy of their completed body chart to the research team.

See **Online** for appendix

For more on the **FotoFinder handyscope patient app** see https://apps.apple.com/au/app/handyscope-patient/id1175303139

	Intervention (n=98)	Control (n=101)	Total (n=199)
Age, years	41·8 (11·8; 19–73)	40·5 (12·6; 18–70)	41·1 (12·2; 18–73)
Sex			
Women	67 (68%)	74 (73%)	141 (71%)
Men	31 (32%)	27 (27%)	58 (29%)
Level of education			
Primary school or leaving certificate	0	2 (2%)	2 (1%)
High school	9 (9%)	12 (12%)	21 (11%)
Trade or technical certificate	16 (16%)	20 (20%)	36 (18%)
University degree or diploma	73 (74%)	67 (66%)	140 (70%)
Relationship status			
Married or cohabiting	76 (78%)	66 (65%)	142 (71%)
Divorced or separated	7 (7%)	11 (11%)	18 (9%)
Single, never married, or not living together	15 (15%)	24 (24%)	39 (20%)
Previous skin spot, mole, or other spot removed or treated			
Yes	60 (61%)	57 (56%)	117 (59%)
No or unsure	38 (39%)	44 (44%)	82 (41%)
First degree relative with a history of melanoma			
Yes	43 (44%)	43 (43%)	86 (43%)
No	55 (56%)	58 (57%)	113 (57%)
Natural skin colour			
Very fair	34 (35%)	28 (28%)	62 (31%)
Fair	53 (54%)	62 (61%)	115 (58%)
Medium	10 (10%)	10 (10%)	20 (10%)
Olive or brown	1 (1%)	1 (1%)	2 (1%)
Eye colour			
Blue, grey, or green-blue	52 (53%)	53 (52%)	105 (53%)
Green or hazel	28 (29%)	27 (27%)	55 (28%)
Brown or black	18 (18%)	21 (21%)	39 (20%)
Completed skin self-examinations			
Baseline	98 (100%)	101 (100%)	199 (100%)
1 month	93 (95%)	101 (100%)	194 (97%)
2 month	81 (83%)	96 (95%)	177 (89%)
Attended clinical skin examination	98 (100%)	101 (100%)	199 (100%)
Type of skin check done during study			
Whole body	69 (70%)	85 (84%)	154 (77%)
Partial body	9 (9%)	6 (6%)	15 (8%)
Skin spots only	20 (20%)	10 (10%)	30 (15%)
Did you have someone assist with checking your skin?			
Yes	70 (71%)	57 (56%)	127 (63·8%)
No	28 (29%)	44 (44%)	72 (36·2%)
Who helped check your skin?			
Partner	59/70 (84%)	49/57 (86%)	108/127 (85%)
Family or friend	9/70 (13%)	5/57 (9%)	14/127 (11%)
Child	1/70 (1%)	3/57 (5%)	4/127 (3%)
Data missing	1/70 (1%)	0	1/127 (1%)

Data are mean (SD; range), n (%), or n/N (%). Some percentages do not sum to 100 because of rounding.

Table 1: **Self-reported participant characteristics**

All participants had an in-person whole-body clinical skin examination by a dermatologist (HPS) within 3 months of their last skin self-examination.

Outcomes

The primary outcomes were sensitivity and specificity of mobile teledermoscopy-enhanced skin self-examination versus naked-eye skin self-examination, compared with the reference standard of whole-body clinical skin examination done by a dermatologist; patient selection of lesions suspicious for melanoma or keratinocyte skin cancers (body sites examined, number of lesions photographed, types of lesion, and lesions missed); and diagnostic concordance of telediagnosis versus in-person whole-body clinical skin examination diagnosis, including histological diagnosis for any excised or biopsied lesions. All primary outcomes and secondary outcomes were analysed in the modified intention-to-treat population, which included all patients who had a clinical skin examination within 3 months of their last skin self-examination. Secondary outcomes were participant satisfaction with services and willingness to pay, which will be reported elsewhere.

Statistical analysis

We anticipated a dropout rate of 5% on the basis of our previous studies.[18,23] Thus, we calculated that a sample size of 110 in each group would be required to provide 80% power (two-tailed) at the 5% significance level to detect an improvement in sensitivity of 20% or higher per lesion by mobile teledermoscopy-enhanced skin self-examination in the lesion-level analysis compared with naked-eye skin self-examination.[24] Such improvement was considered to be clinically relevant and within the upper range of improvements achieved in previous studies investigating skin self-examination aids.[14,15]

Detailed analysis methods have been published previously[21] and the statistical analysis plan is provided in the appendix (p 15). To calculate sensitivity and specificity, lesions that were clinically diagnosed skin cancers or their precursors only (including melanoma, squamous cell carcinoma, Bowen disease or intraepidermal carcinoma, basal cell carcinoma, actinic keratosis, or lesions already excised or biopsied after telediagnosis) were considered positive. Dysplastic or atypical naevi were considered benign lesions. We calculated sensitivity and specificity both at the lesion level and individual level, adjusting for clustering of lesions within participants as previously described by Genders and colleagues.[25] At the lesion level, a skin lesion was counted as true positive if the dermatologist determined the lesion was a skin cancer, requiring treatment, biopsy, or excision at clinical skin examination, and negative if it did not require such interventions. Any lesion that the participant missed that was then found at the clinical visit contributed to the false negative count. The number of true negative (benign) skin lesions per person was calculated on the basis of participants' self-reported response of having none, few, some, or many naevi, and validated clinical whole-body counts, as described by Morze and colleagues.[26] We also did sensitivity analyses by mole count (none [1 mole]; few [around 20 moles];

	Positive on home examination and CSE, n	Positive on home examination and negative on CSE, n	Positive on CSE and negative on home examination, n	Negative on CSE and home examination, n	Concordance	Sensitivity (95% CI)	p value	Specificity (95% CI)	p value
Lesion-level analyses									
Intervention	50	609	17	4355	88%	75% (63–84)	0·04	87% (85–90)	0·42
Control	53	620	7	5011	89%	88% (80–91)	..	89% (87–91)	..
Individual-level analyses									
Intervention	28	4	3	63	93%	87% (76–99)	0·26	95% (90–100)	0·96
Control	31	1	3	66	96%	97% (91–100)	..	96% (91–100)	..

For the lesion-level analyses, data are presented as the number of lesions; for the individual-level analyses, data are presented as number of individuals. Sensitivity and specificity calculations included all lesions clinically diagnosed as melanoma, basal cell carcinoma, squamous cell carcinoma, Bowen disease, intraepidermal carcinoma or actinic keratosis, and lesions already excised or biopsied after telediagnosis. Concordance was calculated using the following equation: true positives + true negatives/total number of lesions (or individuals) × 100. Sensitivity (ie, skin cancer identified during skin self-examination that was also identified by the dermatologist) was calculated using the following equation: (true positive screens/true positive plus false negative screens) × 100. Specificity (ie, skin cancer not identified during skin self-examination with agreement from the dermatologist) was calculated using the following equation: (true negative screens/true negative screens + false positive screens) × 100. CSE=clinical skin examination.

Table 2: **Primary outcomes**

some [around 30 moles]; and many [≥60 moles]) on the basis of the study questionnaire, but the results did not change discernibly (data not reported). At the individual level, if at least one correct positive skin cancer was identified by the participant, a true positive score was given even if one or more other skin cancers were missed, assuming that these lesions would be identified at the clinical skin examination required for the index lesion. Statistical analyses were done using R statistical software. Functions were written and data were analysed using the following methods: χ^2 tests; adjustment of CIs using the ratio estimator; adjustment of CIs using the variance inflation factor; generalised estimating equations (mean sensitivity and specificity averaged across all patients); mixed models (median sensitivity and specificity averaged across all patients); and Gwet's agreement coefficient.

This study was prospectively registered with the Australian and New Zealand Clinical Trials Registry, ACTRN12616000989448.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all of the data and had final responsibility for the decision to submit for publication.

Results

Between March 6, 2017, and June 7, 2018, 484 people responded to the study call, of whom 348 completed the eligibility survey, and 234 were eligible and recruited. Of the 234 enrolled participants, 116 (50%) were allocated to the intervention group and 118 (50%) to the control group. 199 (85%) of 234 participants attended the clinical skin examination and thus were eligible for analyses (figure).

Among the 199 participants in the analysis population, the mean age was 41·1 years (SD 12·2; range 18–73 years), 141 (71%) were women, 117 (59%) had had a suspected skin cancer removed or treated in the past, and 177 (89%) had self-reported a very fair or fair skin type. The groups were well balanced with regard to baseline characteristics (table 1).

Fewer participants in the intervention group completed all three skin self-examinations than did participants in the control group (81 [83%] of 98 participants *vs* 96 [95%] of 101 participants; χ^2=6·56; p=0·01). 69 (70%) of 98 participants in the intervention group reported doing a whole-body skin check compared with 85 (84%) of 101 participants in the control group (χ^2=5·37; p=0·02). 70 (71%) of 98 participants in the intervention group reported they had someone (most commonly a partner) assist with checking their skin compared with 57 (56%) of 101 participants in the control group (χ^2=4·8; p=0·03; table 1).

Participants in the intervention group submitted 615 lesions (median 6·0 per person; range 1–24) once or multiple times for telediagnosis and participants in the control group marked 673 lesions (median 6·0 per person; range 1–16) once or multiple times on the body chart. The proportions of lesions that were photographed by participants in the intervention group that were deemed to require immediate referral by the teledermatologist remained stable across all three timepoints (3·5%; range 3·3–3·9).

At the clinical skin examination, 1376 lesions were assessed by the dermatologist (684 lesions in the intervention group and 692 lesions in the control group), including all participant-selected and dermatologist-selected lesions.

Participants identified 103 suspected skin cancers or precursor lesions (50 lesions in the intervention group

	Lesions missed by participants		Primary diagnosis at clinical skin examination	
	Intervention (n=18)	Control (n=18)	Intervention (n=98)	Control (n=101)
Total number of lesions	25	19	684	692
Predominantly pigmented lesions				
Melanoma*	0	1/19 (5%)	1/684 (<1%)	2/692 (<1%)
Naevus	6/25 (24%)	6/19 (32%)	462/684 (68%)	468/692 (68%)
Lentigo	0	1/19 (5%)	48/684 (7%)	43/692 (6%)
Seborrheic keratosis	0	0	58/684 (8%)	50/692 (7%)
Non-pigmented lesions				
Basal cell carcinoma*	11/25 (44%)	4/19 (21%)	17/684 (2%)	16/692 (2%)
Squamous cell carcinoma*	1/25 (4%)	2/19 (11%)	2/684 (<1%)	4/692 (1%)
Actinic keratosis*	5/25 (20%)	0	37/684 (5%)	28/692 (4%)
Angioma	0	0	11/684 (2%)	5/692 (1%)
Other†	2/25 (8%)	5/19 (26%)	33/684 (5%)	46/692 (7%)
Not diagnosed				
No lesion found	NA	NA	5/684 (1%)	15/692 (2%)
Non-specific	0	0	..	1/692 (<1%)
Removed before exam	NA	NA	10/684 (1%)	10/692 (1%)
Data missing	0	0	0	4/692 (1%)
Body area				
Back	8/25 (32%)	6/19 (32%)	168/684 (25%)	140/692 (20%)
Arms	7/25 (28%)	3/19 (16%)	132/684 (19%)	118/692 (17%)
Chest or abdomen	4/25 (16%)	2/19 (11%)	111/684 (16%)	98/692 (14%)
Legs	1/25 (4%)	5/19 (26%)	111/684 (16%)	145/692 (21%)
Head and neck	4/25 (16%)	2/19 (11%)	111/684 (16%)	157/692 (23%)
Shoulder	1/25 (4%)	1/19 (5%)	31/684 (5%)	20/692 (3%)
Sensitive areas	0	0	19/684 (3%)	14/692 (2%)
Data missing	0	0	1/684 (<1%)	0
Total number of treatments prescribed	25	19	80	93
Excision or shave biopsy	13/25 (52%)	11/19 (58%)	43/80 (54%)	24/93 (26%)
Laser treatment	1/25 (4%)	0	1/80 (1%)	0
Cryotherapy	5/25 (20%)	0	12/80 (15%)	9/93 (10%)
Topical prescription	1/25 (4%)	0	7/80 (9%)	5/93 (5%)
Further monitoring or review	3/25 (12%)	8/19 (42%)	7/80 (9%)	44/93 (47%)
Curette or cautery	0	0	0	1/93 (1%)
Removed before exam	2/25 (8%)	0	10/80 (13%)	10/93 (11%)

Data are n or n/N (%). NA=not applicable. *Skin cancers or actinic keratosis only were used for sensitivity and specificity calculations as reported in table 4. †Other lesions in the control group included myxoid cyst or ganglion cyst (n=1), hyperpigmentation of scar (n=1), insect bite (n=1), benign cyst (n=1), and dermatofibroma (n=1). Other lesions in the intervention group were contact dermatitis (differential diagnosis of parapsoriasis; n=1) and unilateral naevoid telangiectasia (n=1).

Table 3: **Lesions missed by participants and primary clinical diagnosis at clinical skin examination**

and 53 lesions in the control group) at home that the dermatologist deemed to require treatment and missed 24 skin cancers or precursor lesions that were identified by the dermatologist at the clinical skin examination (17 lesions in the intervention group and seven lesions in the control group). At the lesion level, this resulted in sensitivity of 75% (95% CI 63–84) in the intervention group and 88% (95% CI 80–91) in the control group (p=0·04). Specificity was 87% (95% CI 85–90) in the intervention group and 89% (95% CI 87–91) in the control group (p=0·42; table 2).

At the individual level, the intervention group had a sensitivity of 87% (95% CI 76–99) compared with 97% (95% CI 91–100) in the control group (p=0·26), and a specificity of 95% (95% CI 90–100) compared with 96% (95% CI 91–100) in the control group (p=0·96; table 2).

At the clinical skin examination, the dermatologist identified 44 missed lesions on 36 participants that required further monitoring or treatment (25 lesions on 18 [18%] of 98 intervention group participants and 19 lesions on 18 [18%] of 101 control group participants). 20 (45%) of 44 missed lesions (eight lesions in the intervention group and 12 in the control group) did not have a primary diagnosis of skin cancer, but required referral for monitoring, topical treatments, or cryotherapy, and were judged by the dermatologist as worthwhile selecting. The proportion of lesions missed by participants in difficult-to-see areas such as their back was similar between groups (eight [32%] of 25 lesions in the intervention group *vs* six [32%] of 19 lesions in the control group; table 3).

In the intervention group, of the 571 lesions identified at the 1-month skin self-examination, 32 (6%) lesions identified by 19 participants were not rephotographed and 48 (8%) identified by 29 participants were incorrectly photographed by selecting a different lesion than that photographed at baseline (table 4). Of the 511 lesions identified at the 2-month skin self-examination, 26 lesions (5%) identified by 20 participants were not rephotographed, and 29 lesions (6%) identified by 18 participants were incorrectly photographed by selecting a different lesion than that photographed at baseline.

The overall diagnostic concordance between the teledermoscopy and in-person clinical skin examination diagnosis both done by the same dermatologist (HPS) was 88% (Gwet's agreement coefficient=0·88; 95% CI 0·87–0·89), indicating substantial agreement.

Seven participants in the intervention group were asked to visit their general practitioner for treatment on the basis of teledermoscopy findings requiring immediate treatment. At clinical skin examination, 59 (30%) participants (32 intervention group participants with a total of 65 lesions; 27 control group participants with a total of 50 lesions) were asked to visit their doctor for skin lesions requiring treatment found either by the participant or the study dermatologist. Of these, 41 participants required an excision or biopsy for one or more lesions. At the time of analysis (April, 2019), 35 (85%) of 41 of these participants had visited their doctor and 60 skin lesions were excised or biopsied (appendix p 27), of which 44 (73%) of 60 lesions received the same diagnosis as they received at the in-person clinical assessment.

Discussion

Mobile health applications are increasingly used in cancer prevention and early detection, but rarely tested

	Primary diagnosis at baseline SSE	Differential diagnosis at baseline SSE	Primary diagnosis at 1-month SSE	Differential diagnosis at 1-month SSE	Primary diagnosis at 2-month SSE	Differential diagnosis at 2-month SSE
Median (range; IQR)	6·0 (1–24; 4–8)	..	6·0 (1–18; 4–8)	..	6·0 (1–20; 4–8)	..
Total number of lesions	615	51	571	31	511	28
Predominantly pigmented lesions						
Melanoma	0	3 (6%)	0	3 (10%)	0	2 (7%)
Naevus	395 (64%)	9 (18%)	374 (65%)	6 (19%)	340 (67%)	7 (25%)
Lentigo	49 (8%)	5 (10%)	39 (7%)	4 (13%)	34 (7%)	1 (4%)
Seborrhoeic keratosis	98 (16%)	12 (24%)	90 (16%)	7 (23%)	74 (14%)	8 (29%)
Non-pigmented lesions						
Basal cell carcinoma	5 (1%)	6 (12%)	4 (1%)	1 (3%)	3 (1%)	1 (4%)
Squamous cell carcinoma	1 (<1%)	2 (4%)	0	5 (16%)	2 (<1%)	4 (14%)
Actinic keratosis	18 (3%)	6 (12%)	16 (3%)	3 (10%)	10 (2%)	3 (11%)
Angioma	12 (2%)	4 (8%)	9 (2%)	1 (3%)	11 (2%)	1 (4%)
Other*	9 (1%)	4 (8%)	7 (1%)	1 (3%)	6 (1%)	1 (4%)
Not diagnosed						
No lesion found	NA	NA	2 (<1%)	NA	8 (2%)	NA
Not in focus or non-specific	28 (5%)	NA	28 (5%)	NA	19 (4%)	NA
Excised	NA	NA	2 (<1%)	NA	4 (1%)	NA
Lesion photo monitoring						
Change identified	NA	NA	25 (4%)	NA	28 (5%)	NA
No change	NA	NA	463 (81%)	NA	435 (85%)	NA
Incorrect lesion photographed	NA	NA	48 (8%)	NA	29 (6%)	NA
Excised	NA	NA	2 (<1%)	NA	4 (1%)	NA
Photographed for first time	NA	NA	28 (5%)	NA	9 (2%)	NA
Lesion image insufficient quality for change to be determined†	NA	NA	5 (1%)	NA	6 (1%)	NA
Lesions not rephotographed	NA	NA	32 (6%)	NA	26 (5%)	NA

Data are n or n (%), unless otherwise specified. SSE=skin self-examination. NA=not applicable. *Includes warts, skin tags, folliculitis, erythema, focal hyperpigmentation, sebaceous hyperplasia, fibrous papule, excoriated bite, telangiectasia, lichen planus, benign cyst, myxoid cyst or ganglion cyst, neurofibroma, scar, bite or scratch, freckle, photodamaged skin, inflammatory papule, dermatitis, parapsoriasis, fibroma mucous cyst, milia, dermatofibroma, neurofibroma, atypical dermatofibroma, callus, actinic cheilitis, and acne. †At the 1-month SSE, 28 lesions were of insufficient quality to determine a primary telediagnosis; however, of these, 23 could still be used to determine the degree of change from baseline, thus only five lesions were of insufficient quality for the dermatologist to determine whether a change had occurred. At the 2-month SSE, 19 lesions were of insufficient quality to determine a primary telediagnosis; however, of these, 13 could still be used to determine the degree of change from baseline, thus only six lesions were of insufficient quality for the dermatologist to determine whether a change had occurred.

Table 4: **Telediagnosis of submitted lesions at baseline, 1-month, and 2-month self-skin examinations in the intervention group**

stringently for their value with regard to patient care. In this randomised controlled trial, we compared mobile teledermoscopy-enhanced skin self-examination with the currently recommended naked-eye skin self-examination for early detection of skin cancer. Although specificity was high at the lesion level and individual level, and similar between the two groups (>87%), our results did not support the hypothesised 20% increase in sensitivity to detect lesions suspicious for skin cancer, when participants used mobile teledermoscopy compared with conducting a naked-eye skin self-examination. Both the intervention and control groups had high sensitivity (≥75%) for the identification of skin cancers, but the mobile teledermoscopy group missed a higher number of skin cancers (n=17) than did the control group (n=7). Both groups also submitted or marked a large number of benign lesions on their skin, and therefore the proportion of relevant lesions was low in both groups. This reflects the fact that considering the relatively rare event of a skin cancer, the so-called noise-to-signal ratio is high on an individual person's body, and thus considerable precision is required to identify suspicious skin lesions. The introduction of teledermoscopy into clinical practice could lead to a large burden for telediagnostic services if its use results in people submitting many benign lesions. However, automated algorithms excluding clearly benign skin lesions could reduce that burden in the near future.[27]

One reason for lower sensitivity in detecting skin cancers in the intervention group might have been their lower rate of conducting a whole-body skin self-examination (70%) compared with the control group (84%); and lower rate of completing all three skin self-examinations (83%) compared with the control (95%). We postulate that these differences could be due to the time needed to become familiar with teledermoscopy, or the effort required to image and submit each examined lesion via the app. More participants in the intervention group than in the control group reported that they asked

a partner to assist in checking areas of the body that are difficult to see, which might also have affected sensitivity. We did not specifically enquire whether participants shared the study instructions with their partners, and future studies should test whether training for partners could increase sensitivity of teledermoscopy-enhanced skin self-examination. In a previous study, trained partners became deeply engaged in checking areas of the body that are hard to see following skin self-examination training and were more likely to find concerning skin lesions compared with partners who had no training.[28]

Participants in the intervention group more commonly missed basal cell carcinomas (44%) than did participants in the control group (21%). This difference indicates that instructions for using mobile teledermoscopy for imaging basal cell carcinomas require further improvement. In contrast, one case of melanoma was missed by a participant in the control group, whereas no melanomas were missed by participants in the intervention group indicating that the provision of the asymmetry and colour rule via a mobile dermoscopy app was useful to guide intervention group participants towards photographing lesions suspicious of melanoma. In this study, and our previous studies[18,19] when using mobile teledermoscopy, many participants had various skin conditions other than skin cancers that required treatment or follow-up, which would have remained undetected without teledermoscocpy, providing an additional advantage for patients of using this imaging technology.

In this study, up to 5% of images submitted were of insufficient quality for diagnosis, which is considerably lower than estimates from previous studies (20%),[29] indicating the imaging technology is now well advanced and highly usable. In most previous teledermoscopy studies, the imaging process was done by a health professional,[30–32] with only few preliminary studies reported on images taken by the patient themselves or a friend or family member.[17–19] Wu and colleagues and Manahan and colleagues reported concordance between the telediagnosis and in-person clinical diagnosis ranging from 90% to 97% when the patient photographed lesions with a dermatoscope.[17,18] The present study found high management concordance of 88% between in-person and teledermoscopy evaluation, confirming that, if relevant lesions are photographed by participants, they can be triaged by a dermatologist with high accuracy.

In addition to providing information about the value of mobile teledermoscopy, this study is novel in providing evidence from a randomised trial for the value of naked-eye skin self-examination. The trial protocol allowed for stringent follow-up, requiring participants to submit body charts with their findings at three timepoints and to be seen in-person for a whole-body clinical skin examination. Among the control group, at the lesion level, sensitivity was 88% (95% CI 80–91), which is in the upper range of those reported by previous studies (25–93%),[15] indicating that the participants in our study usually selected the correct lesions to show to a doctor, with even higher sensitivity at the individual level. This provides strong evidence for the current public health recommendation for skin self-examination.

This study recruited a volunteer sample who might be more motivated and likely to do a skin self-examination. Most participants were women, with a high level of education, and this study excluded people without an iPhone. Both telediagnosis and clinical diagnosis were done by the same dermatologist, which could have increased estimates of diagnostic concordance between telediagnosis and clinical diagnosis. We did not do a total body lesion count on each participant and true negative calculations were based on self-reported survey data and related clinical count data. We used face-to-face clinical diagnosis as the reference standard instead of histopathology because histopathology is not practical when treatments such as cryotherapy are also used.

Mobile teledermoscopy-enhanced skin self-examination did not result in 20% higher sensitivity than naked-eye skin self-examination for the early detection of skin cancers, thus our hypothesis was rejected. Further improvements to the instructions for participants on the relevance of non-pigmented skin lesions, training for partners, and the integration of automatic algorithms that rule out clearly benign skin lesions at the time of photographing might increase sensitivity of teledermoscopy in the future. Naked-eye skin self-examination seems valuable considering the high sensitivity for suspected skin cancers, and current public health recommendations for regular skin self-examinations should be maintained.

Contributors

MJ, CH, LJL, HPS, JAW, NG, DV, DCW, and BMS contributed to the conception of the study and trial design. MJ, HPS, CH, and UK collected data. MJ and CH drafted the manuscript. MJ, DV, and CH did the statistical analysis. All authors critically revised the manuscript for important intellectual content.

Declaration of interests

RH-W is a founder and shareholder of e-derm-consult. AH reports consulting fees from SciBase, Canfield Scientific, and Aldeyra, during the conduct of the study; and outside the submitted work. HPS reports grants from Medical Research Future Fund; is a shareholder of MoleMap New Zealand and e-derm consult GmbH, and undertakes regular teledermatological reporting for both companies; is a medical consultant for Canfield Scientific and MetaOptima Technology; is a medical adviser for First Derm, and has a medical advisory board appointment with MoleMap New Zealand. All other authors declare no competing interests. FotoFinder Systems GmbH were involved in the development of the mobile teledermoscopy app used in this study.

Data sharing

De-identified and anonymised datasets of clinical trial information will be shared with external researchers for proposals that are complete, for which the scientific request is valid and the data are available, consistent with safeguarding patient privacy and informed consent on publication of this manuscript. A signed data access agreement will be required. The trial protocol and statistical analysis plan are also available in the appendix.

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References

1 Cancer Research UK. Melanoma skin cancer incidence statistics. https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/melanoma-skin-cancer/incidence. (accessed Sept 30, 2019).

2 The Christie NHS Foundation Trust. What is melanoma? https://www.christie.nhs.uk/patients-and-visitors/services/melanoma/what-is-melanoma (accessed Feb 11, 2020).

3 Australian Institute of Health and Welfare. Cancer in Australia: an overview 2014. Canberra: Australian Institute of Health and Welfare. https://www.aihw.gov.au/getmedia/79c940b1-2438-45c8-99e2-a4b593253ccd/18114.pdf.aspx?inline=true (accessed Jan 10, 2020).

4 Venables ZC, Nijsten T, Wong KF, et al. Epidemiology of basal and cutaneous squamous cell carcinoma in the U.K. 2013-15: a cohort study. *Br J Dermatol* 2019; **181:** 474–82.

5 Australian Institute of Health and Welfare. Skin cancer in Australia. 2016. Canberra: Australian Institute of Health and Welfare. https://www.aihw.gov.au/getmedia/0368fb8b-10ef-4631-aa14-cb6d55043e4b/18197.pdf.aspx?inline=true (accessed March 4, 2019).

6 Berwick M, Buller DB, Cust A, et al. Melanoma epidemiology and prevention. In: Kaufman HL, Mehnert JM, eds. Melanoma. Cham: Springer International Publishing, 2016: 17–49.

7 Kandel M, Allayous C, Dalle S, et al. Update of survival and cost of metastatic melanoma with new drugs: estimations from the MelBase cohort. *Eur J Cancer* 2018; **105:** 33–40.

8 Pike E, Hamidi V, Saeterdal I, Odgaard-Jensen J, Klemp M. Multiple treatment comparison of seven new drugs for patients with advanced malignant melanoma: a systematic review and health economic decision model in a Norwegian setting. *BMJ Open* 2017; **7:** e014880.

9 Chambers D, Cantrell AJ, Johnson M, et al. Digital and online symptom checkers and health assessment/triage services for urgent health problems: systematic review. *BMJ Open* 2019; **9:** e027743.

10 Avilés-Izquierdo JA, Molina-López I, Rodríguez-Lomba E, Marquez-Rodas I, Suarez-Fernandez R, Lazaro-Ochaita P. Who detects melanoma? Impact of detection patterns on characteristics and prognosis of patients with melanoma. *J Am Acad Dermatol* 2016; **75:** 967–74.

11 Baade PD, Youl PH, English DR, Mark Elwood J, Aitken JF. Clinical pathways to diagnose melanoma: a population-based study. *Melanoma Res* 2007; **17:** 243–49.

12 Cancer Council Australia. Position statement–Early detection of skin cancer. 2019. https://wiki.cancer.org.au/policy/Position_statement_-_Screening_and_early_detection_of_skin_cancer (accessed March 29, 2019).

13 American Cancer Society. How to do a skin self-exam. 2019. https://www.cancer.org/healthy/be-safe-in-sun/skin-exams.html (accessed Feb 6, 2020).

14 King AJ, Gehl RW, Grossman D, Jensen JD. Skin self-examinations and visual identification of atypical nevi: comparing individual and crowdsourcing approaches. *Cancer Epidemiol* 2013; **37:** 979–84.

15 Hamidi R, Peng D, Cockburn M. Efficacy of skin self-examination for the early detection of melanoma. *Int J Dermatol* 2010; **49:** 126–34.

16 Chao JT 2nd, Loescher LJ, Soyer HP, Curiel-Lewandrowski C. Barriers to mobile teledermoscopy in primary care. *J Am Acad Dermatol* 2013; **69:** 821–24.

17 Wu X, Oliveria SA, Yagerman S, et al. Feasibility and efficacy of patient-initiated mobile teledermoscopy for short-term monitoring of clinically atypical nevi. *JAMA Dermatol* 2015; **151:** 489–96.

18 Manahan MN, Soyer HP, Loescher LJ, et al. A pilot trial of mobile, patient-performed teledermoscopy. *Br J Dermatol* 2015; **172:** 1072–80.

19 Janda M, Loescher LJ, Banan P, Horsham C, Soyer HP. Lesion selection by melanoma high-risk consumers during skin self-examination using mobile teledermoscopy. *JAMA Dermatol* 2014; **150:** 656–58.

20 Janda M, Loescher LJ, Soyer HP. Enhanced skin self-examination: a novel approach to skin cancer monitoring and follow-up. *JAMA Dermatol* 2013; **149:** 231–36.

21 Janda M, Horsham C, Koh U, et al. Redesigning skin cancer early detection and care using a new mobile health application: protocol of the SKIN Research Project, a randomised controlled trial. *Dermatology* 2019; **235:** 1–8.

22 Luttrell MJ, Hofmann-Wellenhof R, Fink-Puches R, Soyer HP. The AC Rule for melanoma: a simpler tool for the wider community. *J Am Acad Dermatol* 2011; **65:** 1233–34.

23 Djaja N, Youl P, Aitken J, Janda M. Evaluation of a skin self examination attitude scale using an item response theory model approach. *Health Qual Life Outcomes* 2014; **12:** 189.

24 Li J, Fine J. On sample size for sensitivity and specificity in prospective diagnostic accuracy studies. *Stat Med* 2004; **23:** 2537–50.

25 Genders TS, Spronk S, Stijnen T, Steyerberg EW, Lesaffre E, Hunink MG. Methods for calculating sensitivity and specificity of clustered data: a tutorial. *Radiology* 2012; **265:** 910–16.

26 Morze CJ, Olsen CM, Perry SL, et al. Good test-retest reproducibility for an instrument to capture self-reported melanoma risk factors. *J Clin Epidemiol* 2012; **65:** 1329–36.

27 Tschandl P, Codella N, Akay BN, et al. Comparison of the accuracy of human readers versus machine-learning algorithms for pigmented skin lesion classification: an open, web-based, international, diagnostic study. *Lancet Oncol* 2019; **20:** 938–47.

28 Robinson JK, Reavy R, Mallett KA, Turrisi R. Remote partner assisted skin self-examination skills training of melanoma survivors and their partners. *Australas J Dermatol* 2019; **60:** e80–82.

29 Rat C, Hild S, Rault Sérandour J, et al. Use of smartphones for early detection of melanoma: systematic review. *J Med Internet Res* 2018; **20:** e135.

30 Markun S, Scherz N, Rosemann T, Tandjung R, Braun RP. Mobile teledermatology for skin cancer screening: A diagnostic accuracy study. *Medicine (Baltimore)* 2017; **96:** e6278.

31 Boyce Z, Gilmore S, Xu C, Soyer HP. The remote assessment of melanocytic skin lesions: a viable alternative to face-to-face consultation. *Dermatology* 2011; **223:** 244–50.

32 Kroemer S, Frühauf J, Campbell TM, et al. Mobile teledermatology for skin tumour screening: diagnostic accuracy of clinical and dermoscopic image tele-evaluation using cellular phones. *Br J Dermatol* 2011; **164:** 973–79.