

“Your Skin Tells You” Campaign for Keratinocyte Cancers: When Individuals’ Selection Makes the Difference

Maria Concetta Fargnoli^{a,b} Paolo Antonetti^{a,b} Laura Atzori^c Paolo Taddeucci^d
Alessandro Di Stefani^{e,f} Vieri Grandi^g Lucia Lospalluti^h Francesco Lacarrubbaⁱ
Sabina Vaccari^j Paolo Amerio^k Gabriella Fabbrocini^l Mariateresa Rossi^m Elena Campioneⁿ
Raffaele Dante Caposiena Caro^o Elvira Moscarella^p Franco Rongioletti^q Cristina Pellegrini^a
Ketty Peris^{e,f}

^aDepartment of Biotechnological and Applied Clinical Sciences, University of L’Aquila, L’Aquila, Italy; ^bDermatology Unit, Ospedale San Salvatore, L’Aquila, Italy; ^cDepartment of Medical Sciences and Public Health, Dermatology, University Hospital of Cagliari, University of Cagliari, Cagliari, Italy; ^dDermatology, University of Siena, Siena, Italy; ^eDermatologia, Università Cattolica del Sacro Cuore, Rome, Italy; ^fDipartimento di Scienze Mediche e chirurgiche, Fondazione Policlinico Universitario A. Gemelli, IRCCS, Rome, Italy; ^gDermatology Section, Department of Human Health Sciences, University of Florence, Florence, Italy; ^hDermatology Unit, University Hospital Policlinico di Bari, Bari, Italy; ⁱDermatology, University Hospital of Catania, Catania, Italy; ^jDermatology Unit, IRCCS Azienda Ospedaliero, Universitaria di Bologna, Bologna, Italy; ^kDermatologic Clinic, Department of Medicine and Aging Science, University “G. d’Annunzio”, Chieti, Italy; ^lSection of Dermatology, Department of Clinical Medicine and Surgery, University of Naples Federico II, Naples, Italy; ^mDermatology Unit, University of Brescia, Brescia, Italy; ⁿDermatology, University of Rome Tor Vergata, Rome, Italy; ^oDermatology Clinic, Maggiore Hospital, University of Trieste, Trieste, Italy; ^pDermatology, University of Campania “Luigi Vanvitelli”, Naples, Italy; ^qIRCCS San Raffaele Hospital, University Vita-Salute, Milan, Italy

Keywords

Awareness campaign · Early detection · Dermatological consultation · Keratinocyte cancers · Prevention · Cutaneous squamous cell carcinoma · Basal cell carcinoma · Actinic keratosis · Nonmelanoma skin cancers

Abstract

Background: Prevention campaigns for skin cancers have focused primarily on melanoma, and over time there has been increasing awareness of the need to select the population to be screened to maximize program effectiveness. **Objectives:** The objective of the study was to report the results of a free dermatological initiative, as part of an awareness

campaign dedicated to keratinocyte cancers, targeting individuals pre-selected through a short questionnaire. **Methods:** One day of dermatological consultations was held at 15 dermato-oncology referral centers during May 22–June 30, 2021. For selection, individuals answered a telephone interview consisting of 7 yes/no questions on risk factors. Demographics, clinical characteristics of suspicious tumors, and histopathologic diagnosis of excised lesions were collected. Suspicion rate, detection rate, and positive predictive values (PPVs) for any skin cancer, basal cell carcinoma (BCC), cutaneous squamous cell carcinoma (cSCC), and melanoma were

Maria Concetta Fargnoli and Paolo Antonetti contributed equally to this work as first authors.

calculated. **Results:** A total of 320 individuals (56.9% males; 43.1% females) with a median age of 69.6 (range 21–91) years qualified for the screening initiative. Overall, skin cancers and precancerous lesions were diagnosed in 65.9% of the patients. Suspicion rate was 28.7% for any skin cancer (92/320), 22.8% for BCC (73/320), 4.7% for cSCC (15/320), and 1.2% for melanoma (4/320). Detection rate was 23.4% for any skin cancer (PPV 93.7%), 18.1% for BCC (PPV 95.1%), 4.4% for cSCC (PPV 93.3%), and 0.9% for melanoma (PPV 75%). **Conclusions:** Selection of individuals at high risk is a cost-effective approach for early detection campaigns for keratinocyte cancers.

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Introduction

Keratinocyte cancers defining basal cell carcinoma (BCC) and cutaneous squamous cell carcinoma (cSCC) are the most common malignancies in humans. They occur in all populations worldwide, but the risk is substantially higher in white individuals, susceptible to UV damaging effects, and in patients older than 60 years [1, 2]. Epidemiological studies have demonstrated a dramatic increase in incidence over recent decades [2], with an estimated 6,350,000 incident cases of nonmelanoma skin cancers and an age-standardized incidence rate of 79.1/100,000 inhabitants in 2019 among 240 countries and territories [3]. However, keratinocyte cancers incidence is likely underestimated and the true burden unclear, mainly because they are not registered by most population-based registries.

BCC and cSCC are a growing public health problem due to an aging population and the aggressive behavior of some histologic subtypes resulting in significant increase of surgical complexity, cancer-related morbidity, and direct costs [4, 5]. Notably, despite the overall favorable clinical outcome of low-risk cSCC, there is a subset of cSCCs that tends to recur and metastasize exhibiting a more aggressive course. The rate of recurrence varies from 2.7% [6] to 4.6% [7] and the rate of metastases ranges from 1.2% to 4%, with 2.1% disease-specific death [7].

Early diagnosis of skin cancers and surgical excision offer the best chance of cure, thus highlighting the need to promote educational programs and early detection initiatives. Screening campaigns for skin cancers applied to unselected populations have shown controversial results in terms of effectiveness and reduction of skin cancer-related mortality, while causing a significant burden on the economic, human, time, and space resources required [8–12]. Systematic reviews and meta-analyses on population-based

skin cancer screening campaigns in both the USA and Europe have concluded that, despite the potential benefits in terms of increasing the detection of early-stage melanoma and nonmelanoma skin cancers, and reducing the incidence and mortality of advanced disease, the strength of evidence for the effectiveness of these campaigns is very low, particularly with regard to cancer-related mortality [8–10]. Indeed, the greater the reduction in mortality, the more advanced the stage of the tumor, while screening campaigns mainly lead to early-stage diagnoses, not without risks of overdiagnosis and consequent psychosocial and aesthetic harm to patients. The lack of conclusive scientific evidence for the effectiveness of skin cancer prevention programs is the main reason why routine screening in the general adult population is not recommended by many organizations worldwide [13].

More recently, the benefits of screening programs have been indeed shown to be greatest among high-risk subgroups or through early access consultation for lesion-directed screening [9, 14]. We report the results of a 1-day free skin-check initiative, as part of an awareness campaign, dedicated to keratinocyte cancers, conducted in Italy during May 22–June 30, 2021, targeting individuals pre-selected through a short questionnaire to increase selectivity in the general population.

Methods

The campaign, entitled “Your Skin Tells You” (in Italian: “Te lo dice la pelle”), was promoted by the Italian Society of Dermatology (SIDeMaST, Italian Society of Medical, Surgical, Aesthetic Dermatology and Sexually Transmitted Diseases) and advertised nationwide through media in the context of an educational and awareness program. Fifteen referral dermatology centers, evenly distributed throughout the country, participated in the campaign: 6 centers in the North, 4 in the center, and 5 in the South and major islands (Sicily and Sardinia). Individuals interested in the initiative could contact a dedicated telephone number. For selection, they answered a brief telephone interview consisting of 7 yes/no questions on risk factors for keratinocyte cancers, detailed in Table 1. If the subjects answered yes to at least 3 of the 7 questions, they meet the criteria for the screening visit. Alternatively, answering yes to any of the following two more relevant questions “Do you have a lesion on your skin that has been bleeding and has not healed for a few months?” and “Do you have a lot of scales/crusts on your face, scalp, or the backs of your hands?” was already sufficient to be enrolled in the screening.

On the scheduled day, a dermatologist performed a total body skin examination using dermatoscopy and noted the clinical diagnosis of the lesions of suspicion and patient data. At the end of the consultation, the patient received a report with the diagnosis of suspicion and related prescriptions (i.e., topical medical therapy, physical therapy, incisional biopsy, or surgical excision).

Table 1. Questionnaire for telephone interview to select high-risk participants^a

1. Are you older than 60 years old?	Yes/no
2. Are you male or female? Male/female; if male, are you bald?	Yes/no
3. Have you had a lesion on your skin for a few months that is bleeding and not healing?	Yes/no
4. Have you ever had a skin cancer removed in the past?	Yes/no
5. Do you spend a lot of time in the sun for work or hobby?	Yes/no
6. Have you had a lot of scales/crusts on your face, scalp, or back of your hands?	Yes/no
7. Do you take immunosuppressive drugs, or have you been treated for lymphoma?	Yes/no

^a If the subjects answered yes to at least 3 of the 7 questions, they meet the criteria for the screening visit. Alternatively, answering yes to question 3 or 6 was already sufficient to be enrolled in the screening.

Each center collected demographic and clinical data of screened participants through a shared database that included the following information: center, patient ID number, sex, age, lesion site, clinical diagnosis, histological examination (yes/no), histopathological diagnosis, others. This study was notified to the Internal Review Board of the University of L'Aquila.

Outcomes

The “suspicion rate” was defined as the number of participants with at least one suspected skin cancer on clinical evaluation (overall, BCC, Csc, or melanoma) divided by the total number of participants. “Positive predictive value” (PPV) was defined as the proportion of histologically confirmed skin cancers among all patients suspected of having skin cancer. The “detection rate” was defined as the proportion of skin cancers correctly diagnosed among all patients screened [15].

Statistical Analysis

Descriptive statistics are given as mean for continuous variables and proportion for categorical data. Participants were categorized as individuals with skin cancer of any type, including BCC, Csc, and melanoma; individuals with actinic keratosis (AK); and individuals with other lesions/no lesions. The Mann-Whitney test and Pearson's χ^2 test were used as appropriate to analyze the suspicion of skin cancer according to sex and age of the participants.

Statistical analysis was realized by the SPSS statistical package (IBM) version 25.0 (SPSS Inc., Chicago, IL, USA). Results were considered statistically significant with a p value of <0.05 .

Results

A total of 2530 subjects contacted the dedicated call center and 320 (12.6%) patients (56.9% male; 43.1% female) qualified for the 1-day skin-check consultation. Of these, 35% (112/320) were recruited in Northern Italy, 27.8% (89/320) in Central Italy, and 37.2% (119/320) in Southern Italy and the major islands, with an even distribution throughout the country. The median age was 69.6 (range 21–91) years, slightly higher in males (71, range 30–89) than females (66, range 21–91) ($p = 0.002$).

Overall, a diagnosis of at least one skin cancer was made in 92/320 patients resulting in a suspicion rate of

28.7%, with a total of 101 lesions suspicious of malignancy (82 BCCs, 15 cSCCs, 4 melanomas) (Table 2). In detail, the suspicion rate was 22.8% for BCC (73/320), 4.7% for cSCC (15/320), and 1.2% for melanoma (4/320). Multiple skin cancers were clinically diagnosed in 8 patients (8/320, 2.5%): 2 or more synchronous BCC in 6 patients, melanoma and BCC or 2 BCC and 2 SCC in 1 patient each. In addition, AKs were detected in 119 (37.2%) patients and 7 patients with BCC had concurrent AK lesions. Finally, 117 benign lesions were diagnosed in all participants.

We further evaluated the association of the diagnosis of suspicion with age and sex of the patient and site of the lesion. A suspicious diagnosis of any skin cancer was significantly associated with older age of participants (72 years, range 28–87, vs. 68 years, range 21–91, $p = 0.002$) but not with sex and site of the lesions (Table 2).

Surgical excision and histopathologic examination were performed in 80 of 101 suspicious skin lesions; the remaining nonbiopsied 21 lesions were superficial BCCs diagnosed by dermatoscopy and treated with topical therapies. Overall, the clinical diagnosis of skin cancer was histologically confirmed in 75 of 80 suspicious lesions (PPV = 93.7%; detection rate = 23.4%). In detail, 58 of 61 clinically diagnosed BCCs were histologically confirmed (PPV = 95.1%, detection rate = 18.1%), as well as 14 of 15 cSCC (PPV = 93.3%, detection rate = 4.4%) and 3 of 4 melanomas (PPV = 75%; detection rate = 0.9%).

Discussion

We report the results of a nationwide educational and awareness campaign with a related free dermatological consultation initiative for keratinocyte cancers in which patients were selected through a short telephone questionnaire on related risk factors in the effort to optimize the effectiveness of the initiative. Overall, skin cancers and precancerous lesions were diagnosed in 65.9% of par-

Table 2. Demographics, diagnosis of suspicion, and anatomical location of suspicious lesions

Demographics and diagnosis of suspicion	Overall, <i>N</i> = 320 (100%)	Female, <i>N</i> = 138 (100%)	Male, <i>N</i> = 182 (100%)	<i>p</i> value
Age (range)	69.6 (21–91)	66 (21–91)	71 (30–89)	0.002
Individuals with AK	119 (37.2)	52 (37.7)	67 (36.8)	0.92
Individuals with suspicious skin cancer of any type	92 (28.7)	35 (25.4)	57 (31.3)	0.21
Individuals with suspicious cSCC	15 (4.6)	5 (3.6)	10 (5.5)	0.42
Individuals with suspicious BCC	73 (22.8)	29 (21.0)	46 (25.3)	0.34
Individuals with suspicious melanoma	4 (1.2)	1 (0.7)	3 (1.7)	na
Anatomical location of suspicious skin cancers	Overall	Female	Male	<i>p</i> value
BCC	82 (100)	30 (100)	52 (100)	0.51
Head/neck	35 (42.7)	12 (40)	23 (35.4)	
Trunk	37 (45.1)	13 (43.3)	24 (46.1)	
Extremities	10 (12.2)	5 (16.7)	5 (9.7)	
cSCC	15 (100)	5 (100)	10 (100)	0.09
Head/neck	8 (53.3)	1 (20.0)	7 (70.0)	
Trunk	–	–	1 (10.0)	
Extremities	7 (46.7)	4 (80.0)	2 (20.0)	
Melanoma	4 (100)	1 (100)	3 (100)	na
Head/neck	1 (25)	0	1 (33.3)	
Trunk	3 (75)	1 (100)	2 (66.7)	
Extremities	–	–	–	

N(%) are presented. AK, actinic keratosis; BCC, basal cell carcinoma; na, not applicable; cSCC, cutaneous squamous cell carcinoma.

Participants with a suspicion rate of malignancy of 28.7%, 22.8% for BCC, and 4.7% for cSCC. Detection rate was 23.4% for all skin cancers, 18.1% for BCC, and 4.4% for cSCC. In recent decades, many prevention campaigns have been conducted focusing primarily on melanoma and only more recently on nonmelanoma skin cancers, with a growing awareness over time of the need to select the population to be screened to maximize program effectiveness.

The German SCREEN project was conducted from July 2003 to June 2004, open to all Schleswig-Holstein residents over the age of 20 and health insurance holders, to evaluate the feasibility of a population-based screening program for both melanoma and nonmelanoma skin cancers. A total of 360,288 participants joined the campaign, with an overall suspicion skin cancer rate of 9.3% and a low detection rate of 0.8% (3,103/360,288) [16].

Euromelanoma is a pan-European project started in 1999 that promotes and shares information on skin cancer prevention, early diagnosis, and treatment, supporting free public screenings during an annual “Euromelanoma Screening Day” in May. In Italy, 5002 unselected patients were screened in 38 public outpatient clinics and private offices by dermatologists during the Skin Cancer

Screening Day in a 3-year period (2005–2007). The overall skin cancer detection rate was 0.64% (32/5,002) with 10 melanomas, 20 BCCs, and 2 SCCs diagnosis [17]. Results of the 2010 Italian Euromelanoma Day enrolling 1,085 participants at 23 centers reported a suspicion rate of all skin cancers of 4.6% and a detection rate of 0.28% for melanoma (3/14), 0.39% for BCC (4/34), and 0.09% for SCC (1/4) [15]. Both studies concluded that, in order to increase the efficacy in terms of early detection, future screening campaigns should focus on selected individuals at high risk for skin cancer and that complete skin examination and the use of dermatoscopy should be encouraged among screening dermatologists.

To identify the right strategy for selecting high-risk patients, Dubbini et al. [18] compared three different methods of recruiting subjects for melanoma screening: (i) regular skin examinations, (ii) occasional melanoma screening during annual public campaigns, and (iii) selective screening for intermediate-/high-risk patients as defined by a self-administered risk evaluation questionnaire. Selective screening performed better than occasional screening, demonstrating that prior assessment of melanoma risk factors allows better selection of a high-risk population for melanoma. However, the suspicion

rate (133/2,238, 5.9%) and detection rate remained low, with pathologically confirmed diagnoses of 2 BCCs and 2 melanomas, for an overall detection rate of 0.18% (4/2,238).

Lesion-directed screening was also shown to optimize skin cancer detection in the general population. In a recent observational study, early-access dermatology consultation for lesion-directed screening after triage by phone resulted in high overall skin cancer and melanoma detection rates [14]. Among the 342 subjects, the skin cancer detection rate was 13.2%. With a history of skin cancer, the detection rate increased to 24.3% while in patients with a negative skin cancer history, the detection rate was 7.7%. Surprisingly, performing total body examination in these patients had only a low additional 0.5% detection rate, and a high number of unnecessary excisions (number needed for excision: 13) [14].

“Your Skin Tells You” was a free dermatological consultation initiative as part of an educational and awareness program for keratinocyte cancers based on a brief selection questionnaire. With the use of a few questions on main risk factors for keratinocyte cancers, with an emphasis on the most significant ones (“Have you had a lesion on your skin that has been bleeding and not healing for a few months?”; “Do you have a lot of scales/crusts on your face, scalp, or back of your hands?”), we obtained an overall skin cancer suspicion rate of 28.7% and detection rate of 23.4%. BCC and cSCC were the most frequent skin cancers diagnosed with few melanomas as compared to other screening programs since the criteria used for our selection were dominated by alerts for keratinocyte cancers. Indeed, we mostly selected individuals older than 60 years, who are less likely to attend screening campaigns but at higher risk for keratinocyte carcinomas. Notably, the use of dermatoscopy during skin examination and the expertise of the screening dermatologists was associated with a very high PPV (93.7% all skin cancers; 95.1% BCC, 93.3% cSCC, 75% melanoma).

In addition, it is important to note that only 320 out of 2,530 (12.6%) individuals qualified as high risk, confirming the low effectiveness of the self-reported approach in prevention campaigns. Triage of self-referrals combined with targeted communication and active invitation of individuals with high-risk factors provide the greatest benefit in increasing early detection of skin cancer by bringing high-risk individuals unaware or uninterested in prevention. Besides the small sample size and the short duration of the screening (only 1 day), which are limitations of our study, the detection rates in our campaign are comparable to those reported for skin cancer screening

campaigns in selected populations but much higher than those reported in the general population.

In conclusion, our results strengthen how selecting participants with a short questionnaire in a keratinocyte cancer prevention initiative is cost-effective by better targeting resources to high-risk individuals. It is conceivable that such questionnaires could be used proactively in education and awareness campaigns to help individuals recognize their risk and increase their interest in prevention.

Key Message

Selection of participants in a keratinocyte cancer prevention initiative is cost-effective by better directing resources to high-risk individuals.

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Statement of Ethics

The study was conducted ethically in accordance with the (<https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/>) World Medical Association Declaration of Helsinki. This study was notified to the Internal Review Board of the University of L'Aquila. No ethics approval and no written informed consent was required, according to Internal Review Board, University of L'Aquila, Palazzo Camponeschi, Piazza Santa Margherita, 2, 67100 L'Aquila (e-mail: irb.segreteria@strutture.univaq.it).

Conflict of Interest Statement

M. C. Fagnoli has served on advisory boards and received honoraria for lectures and research grants from Amgen, Abbvie, Almirall, BMS, Galderma, Kyowa Kyrin, Leo Pharma, Pierre Fabre, UCB, Lilly, Pfizer, Janssen, MSD, Novartis, Sanofi, and Sun Pharma. L. Atzori has served on advisory boards, obtained research grants, and received hospitality for congress from Amgen, Abbvie, Leo Pharma, UCB, Eli-Lilly, Janssen, and Novartis. A. Di Stefani has served on advisory boards and received honoraria for lectures from Galderma, Pierre Fabre, Sanofi, and Sun Pharma. L. Lospalluti has served on advisory boards and received hospitality for congress from Sun Pharma and Amryt. Bristol. F. Lacarrubba has served on advisory boards, received honoraria for lectures, and received hospitality for congress from Abbvie, Almirall, UCB, Novartis, and Sun Pharma. P. Amerio has served on advisory boards and received honoraria for lectures and research grants from Novartis, Lilly, Janssen, Sanofi, and Abbvie. G. Fabbrocini has served on ad-

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Author Contributions

M. C. Fagnoli, P. Antonetti, and K. Peris conceived the presented idea. M. C. Fagnoli, P. Antonetti, C. Pellegrini, and K. Peris analyzed the results and wrote the manuscript. M. C. Fagnoli, P. Antonetti, L. Atzori, P. Taddeucci, A. Di Stefani, V. Grandi, L. Lospalluti, F. Lacarrubba, S. Vaccari, P. Amerio, G. Fabbrocini, M. Rossi, E. Campione, R. D. Caposiena Caro, E. Moscarella, F. Rongioletti, C. Pellegrini, and K. Peris gave substantial contributions to the acquisition of data for the work, contributed to the revision, and agreed with the final version of the manuscript.

Data Availability Statement

All data collected and processed for the study are included and discussed in this manuscript. Further inquiries can be directed to the corresponding author.