Patient-identified early clinical warning signs of nodular melanoma: A qualitative study

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Abstract

Background: Nodular (NM) and superficial spreading melanoma (SSM) show different disease trajectories, with more rapid development in NM and fewer opportunities for early detection often resulting in worse outcomes. Our study described the patient-identified early signs of thin NM via comparisons to *thin* (≤ 2 mm) SSM and *thick* (>2 mm) NM.

Methods: We conducted semi-structured interviews with NM and SSM patients and analyzed the data using thematic analysis.

Results: We enrolled 34 NM and 32 SSM patients. Melanoma early signs uniquely identified by patients with thin NM included white, blue or black coloration, “dot-like” size, fast changes in shape and color observed over 2 weeks, elevation and texture or “puffiness” over 6-12 months, and the sensation that the mole “did not feel right”. Early signs reported by both thin NM and thin SSM patients included round or oblong shape, “jagged” border, pink/red, brown/reddish or dark coloration, “elevated like a pimple” or “tiny bump”, fast color darkening, diameter growth, and border irregularity, and mole feeling “really itchy”.

Conclusions: We found evidence that early signs of NM can be self-identified, which has important implications for the earlier detection of this most aggressive type of melanoma by both health professionals and patients.

Introduction

Melanoma is the most common fatal type of skin cancer, and its incidence continues to rise [1,2]. In the United States melanoma incidence increased from 20.7 per 100,000 in 2001 to 28.2 per 100,000 in 2015 [3]. Superficial spreading melanoma (SSM) and nodular melanoma (NM) are the most frequent subtypes, accounting for 80% of all diagnoses of cutaneous melanoma (CM) [4]. Newer histopathologic classifications of CM define these subtypes as occurring on skin without high cumulative sun damage (CSD), i.e., low-CSD melanoma, and SSM and NM are more likely to harbor the BRAF V600 mutation compared to other melanoma subtypes [5].

Tumour thickness at diagnosis is the key predictor of survival for CM, [6–8] and NM is usually thicker at diagnosis compared to SSM (median thickness at diagnosis: 2.19 – 2.6 mm for NM versus 0.54 - 0.6 mm for SSM) [9,10]. While 90% of SSMs are diagnosed as thin tumours (<= 2 mm; T1/T2) only 20% of NMs are [10], with more than half (56%) of NMs diagnosed at a thicker stage (>2 mm, T3/T4) [9]. Likewise, SSM accounts for 56% of invasive CM diagnoses and 30% of all deaths compared to NM, which accounts for only 14% of invasive diagnoses but 43% of all CM deaths [10]. Prognosis for thin NM is poorer compared to thin SSM [11], with reported rates for disease-free survival ranging from 82% - 84.9% for thin NM versus 91% - 96.4% for thin SSM [12,13], although other studies show similar prognosis when matched for clinicopathologic factors.

Currently, it is unclear whether the increased thickness at diagnosis in NM can be attributed to sex- or age-based differences, e.g., NM tends to be diagnosed more often in males and in individuals 50 years of age and older [12,14,15]; potential delays in diagnosis due to atypical clinical presentation that does not fit general criteria for the early identification of problematic skin lesions [16,17] e.g., the ABCDE rule - asymmetry, border irregularity, uneven color, large diameter (> 6 mm) and evolution [18–20] or the EFG rule - elevated, firm, and growing lesions [21,22]; or whether NM is a biologically distinct, more aggressive subtype of melanoma that grows and spreads faster than other CM subtypes [4,12,23]. What is currently known is that NM tends to elude early clinical detection, with only a minority being detected early (T1/T2 stage) by dermatologists and most being identified later (T3/T4 stage) when melanoma may have already spread to regional lymph nodes [9]. Importantly, more NMs (44%) compared to SSMs (38%) are self-detected or first identified by family or friends as opposed to healthcare professionals[24,25]. These data suggest a critical window of opportunity for early detection, in which patient perspectives can promote understanding of the early clinical signs of NM.

The few studies that have investigated early warning signs of NM versus SSM almost exclusively used quantitative methods either for data collection and/or data analysis (key findings summarized in the Supplementary Materials, Appendix A). As a result, detail about patient-recognized clinical features is limited to questions posed in descriptive, close-ended surveys or the availability of medical records data. Qualitative methods are patient-centered by design and are best suited to investigate patient perspectives on early signs and symptoms of medical conditions, such as melanoma, which develops with visible, pre-clinical signs [19]. Semi-structured interviews can explore patient narratives about early detection in greater depth, including key identifiable features, the circumstances that led to the identification of problematic lesions, and the patient's knowledge base of the condition prior to detection. In addition, the use of prompts and guided questioning can improve patient recall [26].

Research objective

To investigate more thoroughly the early signs of NM from the patient perspective, we conducted a qualitative study with semi-structured interviews focused on producing critical knowledge about mole appearance, observed changes in mole features over time, and sensations experienced about the problematic mole/lesion, as they became apparent to patients in the 12 months prior to diagnostic CM biopsy. This timeline for recall is common in melanoma prevention research and has been previously used to collect data on history of sunburns, sun exposure and practice of skin self-examination [27–31]. As per previous reports, a thickness cut-off of 2 mm was used to differentiate between thinner melanoma (≤ 2 mm, T1/T2) and thicker melanoma (>2 mm, T3/T4). More specifically, we describe the patient-identified early signs of NM via comparisons to *thin* (≤ 2 mm) SSM and *thick* (>2 mm) NM.

Materials And Methods

Study design

The study employed a qualitative design with semi-structured interviews. Semi-structured interviews aim to explore individual viewpoints and the meaning behind people's experiences to give a glimpse into the lived experiences as they occurred prior to theoretical explanations [41]. Individual interviews were conducted to collect patient-driven data addressing the main research questions. The goal was to develop a nuanced and comprehensive understanding of the clinical features of the problematic mole (or lesion) that participants identified on their own prior to receiving a diagnosis of melanoma. Study findings are reported as per the Standards for Reporting Qualitative Research (SRQR) [42]. The 21-item SRQR checklist is included as Supplementary Material.

Participants and procedures

The study was approved by the Institutional Research Board (IRB) of Harvard T.H. Chan School of Public Health and the Research Ethics Board (REB) of McGill University, which are in agreement with the Declaration of Helsinki . **Eligibility** for the study included a confirmed diagnosis of either NM or SSM and receiving treatment at the Masachussets General Hospital between 2012 and 2017. Eligible participants were identified through medical hospital records and included men and women diagnosed with thin (≤ 2 mm) and thick (> 2 mm) NM and SSM. We identified all eligible NM patients (n=109) and matched their profiles by sex, age at diagnosis, and melanoma thickness to SSM patients (1 NM to 3 SSM). The SSM matching pool was chosen randomly from a larger participant pool, as the MGH had disproportionate larger patient samples of SSM compared to NM, as is typical for these melanoma subtypes. Active enrollment occurred between December 2017 and April 2018. The flowchart of participation is included in Figure 1.

Eligible participants received a letter via mail signed by their MGH treating physician informing them about the study and offering an opportunity to opt out of further communication about the study. Subsequently, eligible participants who had not opted out after the initial letter received a study package via mail, which included a brief study description, consent forms, and a brief demographic survey. The cover letter explicitly offered another chance to opt out of further study communication. Participants who had not opted out at this stage, were contacted via phone to discuss enrollment. All participants provided informed consent (verbally over the phone or in writing, by returning signed consent forms) prior to enrollment in the study. We planned to recruit approximately 80 patients (40 NM and 40 SSM) and continued scheduling interviews until we exhausted our sample of consenting participants. We reached out to patients five times before determining that they were inactive.

Data sources

Data were collected via a brief sociodemographic survey and semi-structured interviews. The survey items inquired about key demographic characteristics (education level, age), and health behaviours and attitudes about melanoma prevention and early detection, and were administred with the scope of describing the sample. The interview guide (Supplementary materials, Appendix B) included questions about the appearance of melanoma when initially spotted using prompts that were guided by the ABCDE

criteria [18–20] which identifies problematic lesions by Asymmetry, irregular Borders, varying shades and Colors inside one mole, large Diameter (> 6 mm), and Evolution or changes in any of these criteria. We specifically asked about physical sensations experienced in or around the mole. The time of reference for reporting mole features and changes was 12 months prior to diagnosis. The same set of questions was posed to each participant, with prompts to facilitate recall, which allowed for flexibility to follow up on potentially relevant material. The interviews were conducted over the phone (CM), lasted between 20 and 40 minutes, were audio-recorded using open access software (Open Broadcaster Software), and were transcribed verbatim by a professional transcription service.

Data analysis

Verbatim transcriptions of the interviews were imported into Dedoose [43], a type of software used for qualitative analyses. We used thematic analysis [44] and coded the interview data using an inductive-deductive method whereby a coding manual was created based on the review of the first 10 interviews (deductive approach), which was updated throughout the coding process, as new codes emerged (inductive approach). The initial round of coding was split among three coders (CB, CM, KB). The second round of coding was conducted by another coder (AC) Themes were generated and refined in an iterative fashion throughout multiple team meetings (AC, CM, JD, AG) held between September and December 2019. To ensure the trustworthiness and reproducibility of our findings [45], we used two criteria: *credibility* where the team reviewed the codes carefully in an iterative fashion and agreed on a final set of codes; and c*onfirmability*, where we challenged our own biases by practicing self-awareness throughout the coding process and by challenging personal assumptions during team discussions in which we collaboratively interpreted the data.

Data Synthesis

Data are presented in tabular format. Qualitative findings were summarized according to the established ABCDE criteria [18–20] and also incorporated discrete categories of data described by participants, including a) mole elevation (thickness or depth), b) perceived changes in any of the mole features and the chronology for observed changes; and c) clinical signs and symptoms experienced in or around the problematic mole. In line with the study aims, we used the thin NM group as our reference for contrasts with thin SSM and thick NM groups.

Results

Sample characteristics

The study sample comprised 66 patients: 34 patients diagnosed with NM (thin, n=16; thick, n=18) and 32 patients diagnosed with SSM (thin, n=23; thick, n=9) (see Table 1). Mean time elapsed from diagnosis to interview for the entire sample was 2.56 years (Mean $_{NM}$ = 2.52; Median $_{NM}$ = 2.26; Mean $_{SSM}$=2.42, Median $_{SSM}$=2.71). Patients with thin NM had the lowest mean age at diagnosis (56 versus 59, 61, 63).

Across all four tumour thickness groups, most patients (> 50%) completed college. In addition, the majority of patients (n=56; 85%) were diagnosed with their first melanoma; among patients diagnosed with a second melanoma (n=10), 6 were NMs and 4 were SSMs. Self-reported rates for self-checking for melanoma in the 12 months prior to diagnosis ranged from 56% (thick SSM and thick NM) to 75% (thin NM). Self-reported rates for receiving a medical skin exam in the 12 months prior to diagnosis ranged from 22% (thick SSM) to 65% (thin SSM).

Patients with thin NM reported fewer physical symptoms experienced in the 12 months prior to diagnosis, such as itching, bleeding, irritation, or pain compared to patients with thin and thick SSM or thick NM. Further, there were no reports of tenderness of the mole, discharge or peeling among thin NMs. Half of patients with thin NM self-discovered their melanoma compared to approximately 40% of thin SSM and > 75% of thick NM and thick SSM. Approximately half of patients with thin NM reported some confidence ("somewhat", "quite", or "extremely" confident) in identifying problematic moles compared to 1/3 of patients with thick NMs and thick SSM and ¼ of thin SSM's. More than 3/4 patients from each group self-identified as "generally paying attention to their health". Descriptive statistics are included in Table 2.

A summary of qualitative findings pertaining to the self-identified early signs of melanoma is included in Table 3. For brevity purposes, the thick SSM group (n=9) was not included in the qualitative analysis, as it offered no new information beyond what was already provided by the other two comparison groups, thin SSM and thick NM.

Self-identified early signs of melanoma that are unique to nodular melanoma

With respect to mole appearance, thin NM's stood out in terms of coloration, e.g., "white", "blueish dark", "blueish, multi-colored", or "black", and diameter, e.g., "tiny, tiny, little spot" or "little white dot". In addition, thin NM's reported fast changes in shape, e.g., from "round" to "oblong"; fast changes in color, e.g., from "brownish" to "darker with brown tinges" or from "brown" to "black, in a dripping pattern"; and developed vertical growth over the period of two weeks. Other changes unique to thin NM, which reportedly occurred over the course of several months to one year, included changes in color, e.g., from "blueish dark" to "almost black", and the development of texture, e.g., "became puffy", "puffed up".

Thin NM patients reported elusive tactile sensations, such as "did not feel right, it was purely tactile" compared to more defined signs reported by thin SSM: "hardened, became more solid", and by thick NM: "felt like a hard pimple" or "felt like cracking a peanut open." Bleeding was characteristic of both thin NM and thick NM, with "blood spots under the mole" reported solely by thin NM while "bleeding after shaving or picking at the mole" was reported by both groups. Bleeding was not reported among the thin SSM group.

Self-identified early signs of both nodular and superficial spreading melanoma

Thin NM and thin SSM reported both symmetric e.g., "round", "circular", and asymmetric shape, e.g., "oblong", "like a kidney bean", "not perfectly round, jetted off"; border irregularity, e.g., "a little bit irregular",

“jagged”; coloration in the pink-red-brown range, e.g., “pinkish”, “reddish”, “brownish”, “reddish brown”, “dark”; diameter ranging from “much smaller than a pencil eraser” to “[…] the size of the little fingernail”; and small elevation, e.g., “tiny little bump”, “elevated like a pimple”. Both thin NM and thin SSM reported fast changes in diameter occurring over a few weeks period, and changes observed over the course of six to 12 months in border irregularity, e.g., “got irregular”, color darkening, e.g., from lighter to darker shades of brown, and the development of itchiness, e.g., “itchy”, “really itchy”.

Discussion

Early detection of the more rapidly-growing NM subtype is critical to improved patient outcomes. By the time a patient’s NM shows ABCDE criteria, it is likely to be thicker at diagnosis and less curable. We employed qualitative methodology to facilitate recall of the patient-identified clinical features of problematic moles observed in advance of a formal melanoma diagnosis. This work has important implications for the early detection of NM, which was previously thought to be undetectable at earlier stages.

Our study included 66 patients with NM and SSM, which is the largest and only second[32] qualitative study to date with this population. This study found several patient-identified early signs of melanoma that were unique to thin NM (≤ 2 mm), including small white dot, visible blood spots underneath the mole, blue mole darkening fast, round mole becoming asymmetric fast, mole developing elevation fast, mole becoming puffy and crusty over time, and an overall physical sensation that the mole is different from other moles. Common criteria used for the early identification of melanoma, such as the ABCDE [18–20], elevated-firm-growing (EFG) [21,22] or the blue-black (BB) rule [33] capture some of the early features of NM identified in our study; however, white coloration and very small diameter are not adequately represented in any of these mnemonics.

Additionally, this study found some overlap between the patient-identified early signs of NM and SSM, including round and asymmetric shape, red or brown mole, raised pink bump, darkening of the mole, border becoming irregular, and itchiness developed over time. Symmetric round shape, small diameter (< 6 mm), and itchiness are not captured in the ABCDE criteria; however, elevation or vertical growth are included in the EFG mnemonic, which is typically used to identify NM and less commonly used for the early identification of SSM. A 2003 brief by Kelly and colleagues [21] noted higher percentage of symmetric nodular melanomas (90%) and regular borders and single coloration (78%)- compared to superficial spreading melanoma- and the appearance of a round nodule growing vertically from the onset.

While smaller size diameter and changes in shape, border, color, diameter, elevation and itchiness have been previously reported as features of NM [32,34–36], this is the first study to provide patient-reported chronology for observed changes in mole features. Specifically, among early NMs, changes in mole shape, darkening of color, and rapid vertical growth reportedly occurred over a two week period, accompanied by tactile sensations suggestive of “something different and potentially problematic” about the mole.

Limitations

Given this study asked retrospectively about the early signs of melanoma, there may be a concern about the accuracy of patient recall given the interval between the onset of signs/symptoms and the patient interviews. Prior results from a large nested case-control study investigating the impact of recall bias on effect estimates for various self-reported melanoma risk factors suggested some evidence of bias, with the overall conclusion that the length of time between diagnosis and interview did not systematically affect recall [37]. In a qualitative study asking about retrospective memories, it is virtually impossible to gauge the impact of recall bias. In our study, time from diagnosis to the interview did not differ substantially across the three groups included in the qualitative analysis, thin NM, thin SSM, thick NM, which suggests the accuracy of self-reported data might be comparable across the groups. Notably, results from our written survey show that 5 patients with thin NM (5/16, 31%) reported clinical signs and symptoms. Findings from interview data show that 8 patients with thin NM (50%) reported clinical signs and symptoms: bleeding alone (n=3), itching alone (n=2), itching and bleeding (n=2), and an undefined tactile sensation accompanied by the appraisal that “did not feel right” about the mole (n=1). The discrepancy between the two data sources could be explained by extensive prompts employed by the interviewer to facilitate recall and speak to the relevancy of our qualitative methodology to provide meaningful and personalized information.

Future directions for research

Results from our formative study can guide the development of quantitative measures to assess early detection of nodular and superficial spreading meplanoma, which would allow for the quantification of rates of self-identified early features of melanoma. Our results could also guide future research to develop educational materials about the early detection of various types of melanoma, including the NM subtype, which appears to be more amenable to earlier detection by patients than previously claimed. Further validation of our findings may then warrant revision of existing criteria for earlier clinical recognition of the NM subtype.

Conclusions

Overall, our findings indicate that some of the patient-identified early signs of thin nodular melanoma are not currently ascribed to any of the existing mnemonics used for the early identification of melanoma (ABCDE, EFG, BB rule). These specific features from our findings include the appearance of a small persistent bump or pink pimple, or a tiny round nodule of white, blue, or black color, which feels itchy and undergoes rapid changes in appearance, and “feels” noticeable over a brief two weeks. Incorporation of these findings in melanoma education materials could alert the general public and health care professionals of the key warning signs of nodular melanoma, which is a less common but more fatal melanoma subtype, that has typically eluded early detection strategies and occurs more frequently in older white men [38,39] and across various racial-ethnic groups, such as Hispanic whites [9,40]. Individuals at

high risk as well as healthcare professionals involved in their care particularly benefit from learning about these early signs of nodular melanoma amenable to self-identification.

Declarations

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Conflict of Interests Statement

The authors declare that they have no competing interests.

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Authors' Contribution:

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Formal analysis: AC, CM, CB, KB, AG

Investigation: AC, SS, AG

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

Supplementary Materials

Appendix A: Clinical Features of Nodular Melanoma (NM) and Superficial Spreading Melanoma (SSM), as per Previously Published Reports

Appendix B: Interview Guide

References

1. Little EG, Eide MJ. Update on the current state of melanoma incidence. *Dermatol Clin*. 2012;30(3):355–361.
2. Tripp MK, Watson M, Balk SJ, Swetter SM, Gershenwald JE. State of the science on prevention and screening to reduce melanoma incidence and mortality: The time is now. *CA Cancer J Clin*. 2016;66(6):460-480. doi:10.3322/caac.21352
3. Thrift AP, Gudenkauf FJ. Melanoma Incidence Among Non-Hispanic Whites in All 50 US States From 2001 Through 2015. *JNCI J Natl Cancer Inst*. Published online 2019.
4. Greenwald HS, Friedman EB, Osman I. Superficial spreading and nodular melanoma are distinct biological entities: a challenge to the linear progression model. *Melanoma Res*. 2012;22(1):1-8. doi:10.1097/CMR.0b013e32834e6aa0

5. Elder DE, Massi D, Scolyer R, Willemze R. *WHO Classification of Skin Tumours*. Vol 11. Fourth edition.; 2018.
6. Baade PD, English DR, Youl PH, McPherson M, Elwood JM, Aitken JF. The Relationship Between Melanoma Thickness and Time to Diagnosis in a Large Population-Based Study. *Arch Dermatol*. 2006;142(11):1422-1427. doi:10.1001/archderm.142.11.1422
7. Balch CM, Soong S-J, Gershenwald JE, et al. Prognostic Factors Analysis of 17,600 Melanoma Patients: Validation of the American Joint Committee on Cancer Melanoma Staging System. *J Clin Oncol*. 2001;19(16):3622-3634. doi:10.1200/JCO.2001.19.16.3622
8. Balch CM, Gershenwald JE, Soong S, et al. Final Version of 2009 AJCC Melanoma Staging and Classification. *J Clin Oncol*. 2009;27(36):6199-6206. doi:10.1200/JCO.2009.23.4799
9. Demierre M-F, Chung C, Miller DR, Geller AC. Early Detection of Thick Melanomas in the United States: Beware of the Nodular Subtype. *Arch Dermatol*. 2005;141(6). doi:10.1001/archderm.141.6.745
10. Mar V, Roberts H, Wolfe R, English DR, Kelly JW. Nodular melanoma: A distinct clinical entity and the largest contributor to melanoma deaths in Victoria, Australia. *J Am Acad Dermatol*. 2013;68(4):568-575. doi:10.1016/j.jaad.2012.09.047
11. Dessinioti C, Dimou N, Geller AC, et al. Distinct Clinicopathological and Prognostic Features of Thin Nodular Primary Melanomas: An International Study from 17 Centers. *JNCI J Natl Cancer Inst*. 2019;111(12):1314-1322. doi:10.1093/jnci/djz034
12. Green AC, Baade P, Coory M, Aitken JF, Smithers M. Population-based 20-year survival among people diagnosed with thin melanomas in Queensland, Australia. *J Clin Oncol*. 2012;30(13):1462–1467.
13. Green AC, Viros A, Hughes MCB, et al. Nodular Melanoma: A Histopathologic Entity? doi:info:doi/10.2340/00015555-2855
14. Haenssle HA, Hoffmann S, Buhl T, et al. Assessment of melanoma histotypes and associated patient related factors: Basis for a predictive statistical model. *JDDG J Dtsch Dermatol Ges*. 2015;13(1):37-44. doi:10.1111/ddg.12561
15. Swetter SM, Pollitt RA, Johnson TM, Brooks DR, Geller AC. Behavioral determinants of successful early melanoma detection: Role of self and physician skin examination. *Cancer*. 2012;118(15):3725-3734. doi:10.1002/cncr.26707
16. Cicchiello M, Lin MJ, Pan Y, McLean C, Kelly JW. An assessment of clinical pathways and missed opportunities for the diagnosis of nodular melanoma versus superficial spreading melanoma: Pathways for diagnosis of NM versus SSM. *Australas J Dermatol*. 2016;57(2):97-101. doi:10.1111/ajd.12416
17. Moreau JF, Weinstock MA, Geller AC, Winger DG, Ferris LK. Individual and ecological factors associated with early detection of nodular melanoma in the United States: *Melanoma Res*. 2014;24(2):165-171. doi:10.1097/CMR.0000000000000049
18. Abbasi NR, Shaw HM, Rigel DS, et al. Early Diagnosis of Cutaneous Melanoma: Revisiting the ABCD Criteria. *JAMA*. 2004;292(22):2771. doi:10.1001/jama.292.22.2771

19. Friedman RJ, Rigel DS, Kopf AW. Early detection of malignant melanoma: The role of physician examination and self-examination of the skin. *CA Cancer J Clin*. 1985;35(3):130-151. doi:10.3322/canjclin.35.3.130
20. Rigel DS, Russak J, Friedman R. The Evolution of Melanoma Diagnosis: 25 Years Beyond the ABCDs. *CA Cancer J Clin*. 2010;60(5):301-316. doi:10.3322/caac.20074
21. Kelly JW, Chamberlain AJ, Hospital A, Staples MP, McAvoy B. No longer as simple as ABC. *Aust Fam Physician*. 2003;32(9):706-709.
22. Chamberlain A, Ng J. Cutaneous melanoma: Atypical variants and presentations. *Aust Fam Physician*. 2009;38(7):476.
23. Warycha MA, Christos PJ, Mazumdar M, et al. Changes in the presentation of nodular and superficial spreading melanomas over 35 years. *Cancer*. 2008;113(12):3341-3348. doi:10.1002/cncr.23955
24. Carli P, Giorgi VD, Palli D, et al. Self-detected cutaneous melanomas in Italian patients. *Clin Exp Dermatol*. 2004;29(6):593-596. doi:10.1111/j.1365-2230.2004.01628.x
25. Carli P, De Giorgi V, Palli D, et al. Patterns of detection of superficial spreading and nodular-type melanoma: a multicenter Italian study. *Dermatol Surg*. 2004;30(11):1371–1376.
26. Britten N. Qualitative Interviews. In: *Qualitative Research in Health Care*. John Wiley & Sons, Ltd; 2007:12-20. doi:10.1002/9780470750841.ch2
27. Coups EJ, Geller AC, Weinstock MA, Heckman CJ, Manne SL. Prevalence and Correlates of Skin Cancer Screening among Middle-aged and Older White Adults in the United States. *Am J Med*. 2010;123(5):439-445. doi:10.1016/j.amjmed.2009.10.014
28. Fischer AH, Wang TS, Yenokyan G, Kang S, Chien AL. Association of Indoor Tanning Frequency With Risky Sun Protection Practices and Skin Cancer Screening. *JAMA Dermatol*. 2017;153(2):168-174. doi:10.1001/jamadermatol.2016.3754
29. Geller AC, Emmons K, Brooks DR, et al. Skin cancer prevention and detection practices among siblings of patients with melanoma. *J Am Acad Dermatol*. 2003;49(4):631-638. doi:10.1067/S0190-9622(03)02126-1
30. Geller AC, Keske RR, Haneuse S, et al. Skin Cancer Early Detection Practices among Adult Survivors of Childhood Cancer Treated with Radiation. *J Invest Dermatol*. 2019;139(9):1898-1905.e2. doi:10.1016/j.jid.2019.02.033
31. Vogel RI, Strayer LG, Engelman L, et al. Sun Exposure and Protection Behaviors among Long-term Melanoma Survivors and Population Controls. *Cancer Epidemiol Prev Biomark*. 2017;26(4):607-613. doi:10.1158/1055-9965.EPI-16-0854
32. Bergenmar M, Hansson J, Brandberg Y. Detection of nodular and superficial spreading melanoma with tumour thickness r2.0 mm – An interview study. *Eur J Cancer Prev*. 2002;11:49-55.
33. Argenziano G, Longo C, Cameron A, et al. Blue-black rule: a simple dermoscopic clue to recognize pigmented nodular melanoma. *Br J Dermatol*. 2011;165(6):1251–1255.

34. Bono A, Tolomio E, Carbone A, et al. Small Nodular Melanoma: The Beginning of a Life-Threatening Lesion. A Clinical Study on 11 Cases. *Tumori J*. 2011;97(1):35-38. doi:10.1177/030089161109700107
35. Kalkhoran S, Milne O, Zalaudek I, et al. Historical, Clinical, and Dermoscopic Characteristics of Thin Nodular Melanoma. *Arch Dermatol*. 2010;146(3). doi:10.1001/archdermatol.2009.369
36. Chamberlain AJ, Fritschi L, Kelly JW. Nodular melanoma: Patients' perceptions of presenting features and implications for earlier detection. *J Am Acad Dermatol*. 2003;48(5):694-701. doi:10.1067/mjd.2003.216
37. Parr CL, Hjartåker A, Laake P, Lund E, Veierød MB. Recall Bias in Melanoma Risk Factors and Measurement Error Effects: A Nested Case-Control Study Within the Norwegian Women and Cancer Study. *Am J Epidemiol*. 2009;169(3):257-266. doi:10.1093/aje/kwn363
38. Geller AC, Elwood M, Swetter SM, et al. Factors related to the presentation of thin and thick nodular melanoma from a population-based cancer registry in Queensland Australia. *Cancer*. 2009;115(6):1318-1327. doi:10.1002/cncr.24162
39. Chamberlain AJ, Fritschi L, Giles GG, Dowling JP, Kelly JW. Nodular Type and Older Age as the Most Significant Associations of Thick Melanoma in Victoria, Australia. *Arch Dermatol*. 2002;138(5). doi:10.1001/archderm.138.5.609
40. Pollitt RA, Clarke CA, Swetter SM, Peng DH, Zadnick J, Cockburn M. The expanding melanoma burden in California hispanics: Importance of socioeconomic distribution, histologic subtype, and anatomic location. *Cancer*. 2011;117(1):152-161. doi:10.1002/cncr.25355
41. Kvale S, Brinkmann S. *Interviews: Learning the Craft of Qualitative Research Interviews*. 2nd ed. Sage Publications, Inc.; 2009.
42. O'Brien BC, Harris IB, Beckman TJ, Reed DA, Cook DA. Standards for Reporting Qualitative Research: A Synthesis of Recommendations. *Acad Med*. 2014;89(9):1245–1251. doi:10.1097/ACM.0000000000000388
43. *Dedoose Version 8.0.35*. SocioCultural Research Consultants, LLC www.dedoose.com
44. Braun V, Clarke V. Using thematic analysis in psychology. *Qual Res Psychol*. 2006;3(2):77-101. doi:10.1191/1478088706qp063oa
45. Lincoln YS, Guba EG. *Naturalistic Inquiry*. Sage Publications, Inc.; 1985.

Tables

Table 1. Sample Characteristics

Variable, % (n)	Nodular Melanoma		Superficial Spreading Melanoma	
	≤ 2 mm (n=16)	> 2 mm (n=18)	≤ 2 mm (n=23)	> 2 mm (n=9)
Sex, Female	62.5 (10)	22.2 (4)	52.2 (12)	22.2 (2)
Age at diagnosis, M (SD), Range	56.4 (14.3), 24-81	63.0 (11.4), 44-86	60.7 (17.7), 26-92	58.8 (7.5), 45-71
20-40	12.5 (2)	0.0 (0)	17.4 (4)	0.0 (0)
41-60	43.7 (7)	44.4 (8)	26.1 (6)	66.7 (6)
61-80	37.5 (6)	44.4 (8)	47.8 (11)	33.3 (3)
> 80	6.3 (1)	11.2 (2)	8.7 (2)	0.0 (0)
Highest education completed				
High school or GED	6.3 (1)	22.2 (4)	13.0 (3)	22.2 (2)
Vocational/ Technical	0.0 (0)	0.0 (0)	4.4 (1)	11.1 (1)
College graduate	37.5 (6)	27.8 (5)	39.1 (9)	44.4 (4)
Post-graduate or professional degree	56.3 (9)	50.0 (9)	43.5 (10)	22.2 (2)
Color of skin unexposed to the sun				
Reddish	6.3 (1)	22.2 (4)	9.1 (2)	22.2 (2)
Very pale	25.0 (4)	22.2 (4)	54.5 (12)	11.1 (1)
Pale with beige tint	62.5 (10)	44.4 (8)	31.8 (7)	33.3 (3)
Light brown	6.3 (1)	11.1 (2)	0.0 (0)	33.3 (3)
Dark brown	0.0 (0)	0.0 (0)	4.5 (1)	0.0 (0)
First melanoma Yes	75.0 (12)	88.9 (16)	82.6 (19)	100.0 (9)
Skin self-exam during the 12 months prior to diagnosis?				
No	25.0 (4)	44.4 (8)	34.8 (8)	44.4 (4)
Yes, whole body exam	25.0 (4)	16.7 (3)	13.0 (3)	11.1 (1)
Yes, partial exam	50.0 (8)	38.9 (7)	52.2 (12)	44.4 (4)
Medical skin exam during the 12 months prior to diagnosis?				

Variable, % (n)	Nodular Melanoma		Superficial Spreading Melanoma	
	≤ 2 mm (n=16)	> 2 mm (n=18)	≤ 2 mm (n=23)	> 2 mm (n=9)
No	37.5 (6)	38.9 (7)	34.8 (8)	77.8 (7)
Yes, whole body exam	56.3 (9)	33.3 (6)	47.8 (11)	22.2 (2)
Yes, partial exam	6.3 (1)	27.8 (5)	17.4 (4)	0.0 (0)
Who performed the medical skin exam				
Dermatologist	37.5 (6)	38.9 (7)	47.8 (11)	22.2 (2)
PCP or another HCP	25.0 (4)	27.8 (5)	17.4 (4)	0.0 (0)

Note. PCP = primary care provider; HCP = health care provider

Table 2. Self-report Survey Variables Crosstabulated by Melanoma Type and Depth

Variable, % (n)	Nodular Melanoma		Superficial Spreading Melanoma	
	≤ 2 mm (n=16)	> 2 mm (n=18)	≤ 2 mm (n=23)	> 2 mm (n=9)
Physical signs in 12 months pre- diagnosis (*checked all that apply**)				
Itching	12.5 (2)	22.2 (4)	17.4 (4)	44.4 (4)
Bleeding	12.5 (2)	22.2 (4)	17.4 (4)	44.4 (4)
Irritation**	12.5 (2)	33.3 (6)	4.3 (1)	66.7 (6)
Tenderness**	0.0 (0)	38.9 (7)	4.3 (1)	55.6 (5)
Pain**	6.3 (1)	33.3 (6)	4.3 (1)	55.6 (5)
Discharge	0.0 (0)	5.6 (1)	4.3 (1)	11.1 (1)
Peeling	0.0 (0)	33.3 (6)	4.3 (1)	11.1 (1)
Who discovered the melanoma?				
Self or partner	50.0 (8)	76.5 (13)	39.1 (9)	87.5 (7)
Friend or colleague	0.0 (0)	11.8 (2)	8.7 (2)	0.0 (0)
Primary care physician	12.5 (2)	0.0 (0)	13.0 (3)	0.0 (0)
Nurse or physician assistant	0.0 (0)	0.0 (0)	4.3 (1)	0.0 (0)
Dermatologist	31.3 (5)	5.9 (1)	26.1 (6)	0.0 (0)
Another professional	6.3 (1)	5.9 (1)	8.7 (2)	12.5 (1)
Confidence differentiating healthy and problematic moles?				
Not at all confident	25 (4)	44.4 (8)	17.4 (4)	33.3 (3)
A little confident	18.8 (3)	22.2 (4)	47.8 (11)	33.3 (3)

Variable, % (n)	Nodular Melanoma		Superficial Spreading Melanoma	
	≤ 2 mm (n=16)	> 2 mm (n=18)	≤ 2 mm (n=23)	> 2 mm (n=9)
Somewhat confident	18.8 (3)	11.1 (2)	13.0 (3)	22.2 (2)
Quite confident	31.3 (5)	16.7 (3)	13.0 (3)	11.1 (1)
Extremely confident	6.3 (1)	5.6 (1)	8.7 (2)	0.0 (0)
“I am someone who pays attention to my health”				
Disagree	0.0 (0)	5.6 (1)	0.0 (0)	22.2 (2)
Neither agree or disagree	12.5 (2)	22.2 (4)	17.4 (4)	0.0 (0)
Agree	31.3 (5)	50.0 (9)	39.1 (9)	33.3 (3)
Strongly agree	56.3 (9)	22.2 (4)	43.5 (10)	44.4 (4)

Note.

*The percentages do not add to 100% within each thickness group because the respondents were instructed to select all of the symptoms they had experienced from a list of possible symptoms.

**We found statistically significant differences between the four thickness groups.

Table 3. Perceived Early Signs and Symptoms of Melanoma

Signs/ symptoms	Nodular melanoma	Superficial spreading melanoma	Nodular melanoma
	≤ 2 mm	≤ 2 mm	> 2 mm
Asymmetry			
Round	Round or roundish, circle or circular	Circular, like a big circle	Circular, like a big circle
Oblong	Not perfectly round, oblong	Not perfectly round, jetted off	
	Like a small kidney bean	Not perfectly round, smaller in one direction	
Square	Square		Rectangular
Border			
Slightly irregular	A little bit (or slightly) irregular	Half-moon edge on the side of the border	A little irregular
			Definite border, visible where it started and stopped
Jagged	Jagged	Jagged border on one side	
		Jagged, uneven, undefined, melted into skin	
Irregular coloration		Skin was a little bit pink, right on the border	
		[Pinkish with] a tan border	
Color			
White	Little white dot		Interior looked white or grey-white
			Brownish white
			Darker white
Beige	Very light beige w/ black spot in the middle		Skin color shade
Blue	Bluish dark		
	Bluish, multi-colored		
Black	Black freckle, like a black head		

Signs/ symptoms	Nodular melanoma	Superficial spreading melanoma	Nodular melanoma
	≤ 2 mm	≤ 2 mm	> 2 mm
	Black dotted marks leaving a trail of brown		
Pink	Pinkish, looking like a pimple	Pinkish	Pink
		Pinkish with a tan border	
		Pinkish, pearlescent- like a reflection of a pearl	
		Pink bumpy/bubbly area with a black freckle on top	
			Dark pink
Red	Red		Red
	Red, pinkish lesion	Reddish	Reddish, almost bright red
	Tiny, little red spot		
Brown		Light and dark brown, with darker spots inside	
	Brown	Brown	Brown
	Brownish or maroonish	Brownish like a dark freckle	A little brownish
	Brownish dark		Dark brown
Reddish brown	Dark, reddish brown	Brown and lighter /reddish	Brown with some red
		Reddish brown	Brown with some purple
Dark	Really dark with an even darker spot inside	Dark, almost black	Dark
Diameter			
Tiny dot	Like a dot made with a pen	Tiny, like lead on a pencil, the size of a dot	
	Tiny, tiny little spots		
	Tiny, tiny, tiny, like the head of a pin		

Signs/ symptoms	Nodular melanoma	Superficial spreading melanoma	Nodular melanoma
	≤ 2 mm	≤ 2 mm	> 2 mm
	Like if you took a fine-tipped pen and you just put three dots on a piece of paper		
< Pencil eraser	Fairly small (1/8 of an inch)	Very small (2 mm to 3-4 mm)	Like a small pinhead used for sewing (1.5 mm)
	Much smaller than a pencil eraser	Much smaller than a pencil eraser	Like the tip of a pen (2 mm)
	Like a half of a pencil eraser	Smaller than the size of a pencil eraser	
	About 2/3 of a pencil eraser	Half the size of a pencil eraser, very small	
~ Pencil eraser	The size of a pencil eraser	Almost the size of a pencil eraser	The size of a pencil eraser
		The size of a pencil eraser or a little smaller	Like a big pimple (1/4 of an inch
			About 1/4 inch round
> Pencil eraser	A little bigger than a pencil eraser	Like two pencil-head erasers side-by-side	A little bigger than the size of a pencil eraser
	The size of my little finger's fingernail	The size of the little fingernail on your hand	As big as a very small blueberry, maybe even smaller
	Really tiny, smaller than 1 cm	1 cm diameter	
		Smaller than the size of a dime	
		A little bit smaller than my thumbnail	The size of my thumbnail
		About the size of a dime, maybe bigger	About the size of a dime
			The size of a penny
			The size of a quarter, large

Signs/ symptoms	Nodular melanoma	Superficial spreading melanoma	Nodular melanoma
	≤ 2 mm	≤ 2 mm	> 2 mm
			A little bigger than a quarter
			Approximately 2 cm
Elevation			
Slight	Teeny little bump	A little raised (1/8 of an inch; 1 mm)	A little raised
	Only slight [elevation]	Elevated a little, you could feel it, definitely	A little raised bump
	Not huge, just slight [elevation]	Could feel it- if you ran your finger over it	A little bit raised but not grossly
	Definitely more flat, but [also] raised a bit	Not very much elevated, a little bumpy	Elevated a little bit
	Flat, less than 1 mm, a really tiny thing	Like a little raised scar, bubbly a little bit	A little bit elevated, some parts higher than others
	A little bit elevated but small, small	Rounded at the top, a tiny bubble like a tiny curve - also went down below the surface	Could feel it, wasn't flush with the skin (1/4 inch high)
	Elevated above the skin like bumps on skin		The big the balloon was maybe 1/8 of an inch
	Elevated, like a pimple		Raised at least a ¼ of an inch, maybe more
Textured	A little bit raised, puffy, just like a little bump	A little bit bumpy with a rough texture	Growing out of the skin, I could feel the crustiness
	A little bit raised, puffed up	A little raised, a little crusty	Felt like a bee sting, no pain (the texture of it)
Prominent	Raised up and prominent		Raised, pronounced, thick (5 mm)
			Raised, like a swelling from a bee sting

Signs/ symptoms	Nodular melanoma	Superficial spreading melanoma	Nodular melanoma
	≤ 2 mm	≤ 2 mm	> 2 mm
Evolution ***[chronology]***			
Asymmetry change	From round to oblong *[2 weeks]*	Changed shape *[In a matter of weeks]*	Looked different from last time I checked *[2 months]*
		Not the same shape as in the past *[6 months]*	
Border change	Became more irregular *[6-12 months]*	Got irregular *[In a matter of weeks]*	
		Some parts of the border became red *[Over the last few years]*	
Color change	From light beige to beige with a black spot *[Over time]*	Became darker at the center	
	From brownish to darker with brown tinges *[2 weeks]*	From light brown to really dark *[Really fast]*	
		Got darker, from light to dark brown *[6 months]*	
	Became a little bit dark	Got a little darker *[Slowly, over the years]*	
			From brown to brown with purple in it *[2-4 months]*
	From brown to black, in a dripping pattern *[2 weeks]*		From brown to black *[4-5 months]*
	From bluish dark to almost black *[3 months]*		Blackened
Diameter change	Didn't get too much bigger *[2 weeks]*	Grew in size *[Overnight]*	Got bigger, from 0.5 to 2 cm *[4 weeks]*
	Grew quickly, all of a sudden *[4-6 weeks]*	Got a little bigger *[Over the last few years]*	Got bigger *[3-4 months]*
	Got a little bit bigger, larger *[3 months]*	Grew a little bit bigger *[Slowly, over the years]*	Came back/grew after biopsy *[4-5 months]*

Signs/ symptoms	Nodular melanoma	Superficial spreading melanoma	Nodular melanoma
	≤ 2 mm	≤ 2 mm	> 2 mm
	Got bigger, from 1 to 2 mm *[6-12 months]*	Grew in size, from nothing to pencil eraser size *[In a matter of weeks]*	Got slightly bigger *[Almost 1 year]*
	Got (a little bit) bigger *[Over time]*		Kept getting bigger and bigger
	Growing in size *[12 months]*		
Elevation change	Got raised *[2 weeks]*		Got higher *[4 weeks]*
			More raised *[2 months]*
		Got more density to it *[Very quick]*	Became thicker *[3.5 weeks]*
	Became more pronounced		Became more pronounced, protruding from the skin *[Relatively quickly]*
	Became puffy *[6-12 months]*		Became bumpier, not smooth *[2-4 months]*
	Puffed up *[Over time]*		
Physical signs and symptoms			
Itchy	A little bit itchy		
	Really itchy	Itching a good deal	
	Became itchy	Became itchy *[6 months]*	Became itchy *[2 months]*
Bleeding	Bleeding after shaving/ picking at it		Bleeding after shaving or squeezing *[2-3 weeks]*
	Blood spots under the mole		Bleeding
Weeping			Weeping pus
			Discharge

Signs/ symptoms	Nodular melanoma	Superficial spreading melanoma	Nodular melanoma
	≤ 2 mm	≤ 2 mm	> 2 mm
			Moist
Multiple signs	A little bit itchy and bleeding *[Once]*	Itchy, scaling and flaky, cracking, bleeding	Itchy, sore/sensitive, and bleeding- from towel drying
			Bleeding a little, open sore, scabbed over
		A little bit itchy and a little bit scaly	Itchy and erupting *[Periodically]*
		Itchy, did not heal, looked like a keloid scar	
		Became dry, scaly, peeling *[All of the sudden]*	
		Sensitive and hurting/ sore, radiating pain *[All of a sudden]*	Itchy and painful
			Oozing- from towel drying, sensitive, breaking open
Tactile sensations	Did not feel right, it was purely tactile		Could feel it- by touching
		Hardened, became more solid *[Over a few days]*	Hardened a little bit
			Felt like a hard pimple- by touching
			Felt like cracking a peanut open- after squeezing

Note. NM = nodular melanoma; SSM = superficial spreading melanoma.

Figures

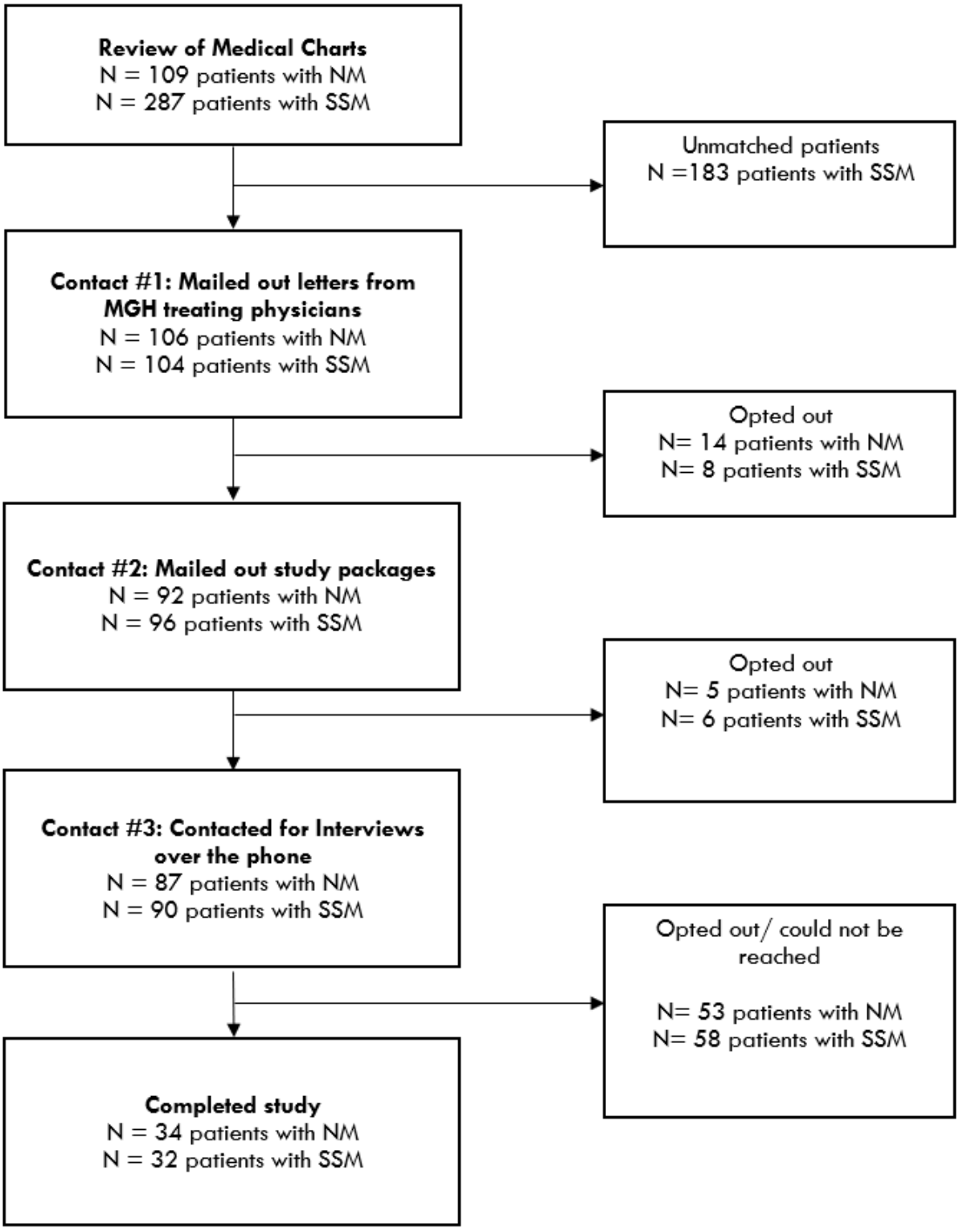

Figure 1

Study flowchart detailing study selection, enrollment, and completion. Legend. NM = nodular melanoma; SSM = superficial spreading melanoma; MGH = Masachussetts General Hospital

Supplementary Files

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- SRQRchecklist.JID.2021.02.17.docx
- SupplementaryMaterials.docx