



Treatment Patterns, Outcomes, and Patient Satisfaction of Epidermal Superficial Non-Melanoma Skin Cancer at an Academic Dermatologic Surgery Center

Citation

Drew, Benjamin. 2015. Treatment Patterns, Outcomes, and Patient Satisfaction of Epidermal Superficial Non-Melanoma Skin Cancer at an Academic Dermatologic Surgery Center. Doctoral dissertation, Harvard Medical School.

Permanent link

<http://nrs.harvard.edu/urn-3:HUL.InstRepos:17295900>

Terms of Use

This article was downloaded from Harvard University's DASH repository, and is made available under the terms and conditions applicable to Other Posted Material, as set forth at <http://nrs.harvard.edu/urn-3:HUL.InstRepos:dash.current.terms-of-use#LAA>

Share Your Story

The Harvard community has made this article openly available.
Please share how this access benefits you. [Submit a story](#).

[Accessibility](#)

TABLE OF CONTENTS	PAGE NO.
TITLE PAGE	1
ABSTRACT	1
TABLE OF CONTENTS	2
GLOSSARY OF ABBREVIATIONS	3
SECTION 1	
- INTRODUCTION	4-6
SECTION 2	
- METHODS	7-8
SECTION 3	
- RESULTS	9-10
SECTION 4	
- DISCUSSION	11-12
- LIMITATIONS	12
- CONCLUSIONS	12
- SUGGESTIONS FOR FUTURE WORK	13
LIST OF REFERENCES	14-16
TABLES AND FIGURES	17-21
APPENDICES	22-24

GLOSSARY OF ABBREVIATIONS

ANOVA

analysis of variance

BCC

basal cell carcinoma

CI

Confidence interval

CM

Centimeters

ED&C

electrodessication and curettage

HR

hazard ratio

IBD

inflammatory bowel disease

MMS

Mohs micrographic surgery

NMSC

non melanoma skin cancer

OTR

organ transplant recipient

PDT

photodynamic therapy

RA

rheumatoid arthritis

SCC

Squamous cell carcinoma

SCCIS

squamous cell carcinoma in-situ

SD

standard deviation

INTRODUCTION

Non melanoma skin cancer (NMSC), comprised predominantly of basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), is the most common malignancy in the United States.¹ Epidermally limited skin cancers such as superficial BCC (sBCC) and squamous cell carcinoma in-situ (SCCIS) may account for 30% of BCCs and 12% of SCCs, respectively.²⁻⁴ At present, an estimated 3,500,000 cases of NMSC are diagnosed annually, making superficial skin cancer more common than the cumulative incidence of lung, breast, prostate, and colon cancer.^{1,5} Based on current epidemiological trends, the incidence and prevalence of NMSCs continues to rise.¹ With increasing surveillance, 20% of adults are projected to receive the diagnosis within their lifetime.⁶

NMSC is routinely not tracked with other cancers and is not included among discussions or publications of cancer statistics, largely due to the fact it does not convey a high mortality.¹ However, as a result of its rising incidence and prevalence, it is levying a burden onto the financial viability of our health care system.⁷⁻⁹ In fact, its treatment and management account for a substantial cost to the US health-care system, with annual estimates exceeding 4.5% of all cancer treatment care expenditures.^{5,10} The average annual total cost of NMSC is estimated to be about \$4.7 billion.¹¹ As the population ages, the number of enrollees in Medicare will also grow considerably in the next 20 years, raising considerable concerns over the anticipated costs of providing care to a burgeoning elderly population. This will likely have a sizable impact on NMSC care because NMSC is generally an affliction of older age and Medicare assumes the majority of cost coverage for NMSC treatment in the United States.²⁴

Presently, a broad array of treatment modalities exist for these epidermally-limited skin cancers, which include excisional surgery, electrodesiccation and curettage (ED&C), photodynamic therapy (PDT), cryotherapy (CT), radiation, topical pharmacotherapy (TM) (5-Fluorouracil, Methotrexate, Imiquimod), and Mohs micrographic surgery (MMS).¹²⁻¹⁴ Despite research to evaluate the efficacy of these modalities, a consensus has not yet materialized as to which treatments are optimal.^{15,16} Instead, significant variation in treatments for invasive and superficial NMSC abound.^{12,17}

At present, it is important to note that there are also newer targeted biomolecular therapies for cutaneous NMSC in developmental and clinical trial phases.¹⁸ In fact, blockade of the hedgehog signaling pathway has been a breakthrough in the management of BCC as has epidermal growth factor receptor inhibition for SCC.¹⁹ As these novel and costly therapies emerge, it will be even more important to understand the efficacy of existent treatment modalities in order to fully enumerate their cost efficacy and therapeutic utility.

Originally conceived in the 1930s by Federic Mohs, MMS is a complicated modality that involves serial excision of a tumor followed by microscopic evaluation of the tissue margins.²⁰ The practice of MMS has become a widely adopted and recommended standard of treatment for epidermally limited NMSC. The technique has also incrementally evolved from the procedure performed by its original architect, which could take days to complete. Current MMS procedures are performed expediently in a single visit and have capitalized on new imaging

techniques such as immunohistochemistry and confocal microscopy.²¹ The histologic verification of tumor removal is the basis for its creditable results in achieving higher clearance and lower recurrence rates than other NMSC treatment modalities. Retrospective analysis reveals there has been upward trend in the use of MMS, particularly in the head and neck region where tissue preservation is important.²²

Topical chemotherapeutics (TM) provide a cytotoxic treatment approach for cases involving multifocal lesions, unclear lesion boundaries, risk of keloids, comorbid surgical risk factors, and concern for cosmetic outcomes secondary to surgery.²³ Cryotherapy, in the form of liquid nitrogen spray, is an alternative to topical chemotherapeutic agents that is inexpensive, widely available, and relatively simple to administer. Although the superficial therapies such as topical pharmacotherapy and cryotherapy are generally associated with lower clearance rates and higher recurrences, the data to support this assertion remains limited.^{24,25} Furthermore, there is need for additional scrutiny of treatment modalities with a specific focus on longer term follow-up and comparison with surgical outcomes.²⁶

Given the recent public attention in the news media, regarding the increasing reliance on MMS, there is also a growing concern over the higher cost of histologically guided tumor removal surgery.²⁷ Even after adjusting for risk factors and inflation, the more labor intensive MMS is associated with higher fees than procedures such as cryotherapy, ED&C, and topical treatments.²⁸⁻³² Amidst increasing scrutiny of the necessity and cost of dermatologic treatment modalities, further research is required to assess treatment efficacy.

There is also a growing recognition within the medical marketplace that health care must be responsive to patients' preferences and unique needs, especially given the evolving trend towards managing chronic diseases that require longer health care interventions.³³ Enhancing patient satisfaction may therefore be significantly more important since it may precipitate better compliance with treatment and deliver superior health outcomes.³³ With nascent research that links patient satisfaction to better health outcomes and the expanding emphasis on patient-oriented health care delivery, further study is needed to assess patient satisfaction associated with superficial BCC and SCCIS care. Overall short- and long-term satisfaction has incrementally been studied and linked to age, skin-related quality of life, disease severity, mental health, treatment type, the time a physician spends with a patient, and a physician's interpersonal skills.^{33,34} While several patient centered satisfaction investigations of NMSC have previously been undertaken, these studies have focused entirely on dermatologic surgery.³⁴⁻³⁷ Consequently, insufficient data exists on patient satisfaction for the various treatment modalities of NMSC and notably, none have provided an analysis of patient satisfaction with superficial treatments such as topical chemotherapy or cryotherapy. Furthermore, based on a review of current literature, there have been no studies that have specifically considered a patient's concern for recurrence or willingness to undergo treatment again, both of which are practical considerations in the clinical setting for a provider who is confronted with the decision of which treatments to discuss, recommend, and render.

Based on comparison of recurrences and post-treatment satisfaction, this research endeavors to provide a foundation for more detailed comparative effectiveness studies and a justification for using less costly treatments, which is increasingly important in terms of

delivering higher quality, evidence based care in an increasingly resource constrained and patient centered care environment. With the growing emphasis placed on personalized healthcare, this study will also serve to elucidate which treatment modalities provide the highest level of satisfaction, which can serve as an education and counseling tool for clinicians in the pre-operative setting when patients are confronted by a multitude of treatment options, confusing choices, and concerning health outcomes. Finally, these results may enable other skin cancer and dermatologic surgery centers to reassess their algorithms for treatments offered and rendered.

Research Aims

The objectives of this study are to:

1. retrospectively evaluate treatment patterns for a cohort of patients with a pre-treatment diagnosis of sBCC and SCCIS at an academic center that performs MMS.
2. investigate whether differences exist in efficacy and outcomes of various treatment modalities, as measured by recurrence rates
3. identify prognostic factors for tumor recurrence, and
4. evaluate patient satisfaction with various treatment modalities for epidermally limited NMSC

METHODS

The Mohs and Dermatologic Surgery Center database was searched for all patients treated for sBCC and SCCIS between January 2008 and March 2014 by two physicians at an academic affiliated dermatologic surgery center in Boston, MA. Tumors considered suitable for inclusion of the study included superficial BCC and SCCIS on any location of the body. Using clinical, operative, and pathology notes from an electronic health record, the medical histories and encounters of these patients were reviewed and recorded using a structured data collection form. The information documented included demographic data (age, sex, Fitzpatrick skin type, immunosuppressive status, reason for immunosuppression); tumor characteristics (histopathologic subtype, location, size dimensions, date of consultation, date of treatment, and duration of follow-up); treatment modality discussed and rendered; treatment effectiveness (complete response, incomplete response, and recurrence); and post-treatment complications (bleeding, hypersensitivity reactions, infection, actinic keratosis, and poor wound healing). For topical chemotherapeutic treatments, type of medication, frequency of application, and duration of prescribed treatment was recorded. With regard to Mohs micrographic surgery, additional data included total number of stages before reconstruction, post-operative defect size, and reconstruction type. Patients were excluded if they received a combination of two or more therapies, failed to adhere to the prescribed treatment plan or refused treatment.

Of note, some patients included in this study exhibited multiple NMSCs warranting treatment. Each skin lesion was included as an individualized data point. For example, if a patient presented with 2 lesions (a BCC on his forehead and a SCCIS on his neck), this patient was categorized as two separate data points in the study.

From the study's cohort, a 25% subset from each treatment group was randomly selected to participate in a retrospective patient satisfaction survey from May 2014 to June 2014. Patient recruitment letters and surveys (see Appendix 2 and 3) were mailed to prospective participants. Approximately two weeks after dispatching the letters, patients were contacted over the telephone by trained research staff to obtain consent and verify patient recall of the tumor diagnosis, location, date of treatment, and treatment administered. After obtaining verbal consent, a survey was administered, via the telephone. Four questions were posed about overall level of satisfaction, concern for recurrence, current status of treatment site, and willingness to accept their previous treatment, if required (see Appendix 3). For overall satisfaction, the patient was asked the following question: "Overall, how satisfied were you with your treatment?" Answers provided by patients were limited to "Very Satisfied, Satisfied, Not Satisfied, or Very Dissatisfied." Each answer was linked with a score of 4 to 1, with a high mark correlated to an increased satisfaction with their medical treatment. For the next 3 questions, patients' answers were dichotomized to "Yes" or "No." If patients were not accessible on the first attempt, two additional attempts at different times on subsequent days, over the course of 2 weeks, were undertaken to solicit the patient's participation. Patients were excluded if they were unwilling to consent, unable to recall their treatment, cognitively impaired, not fluent in English, or were not accessible over the phone. Additional patients were randomly selected from the cohort to participate in the questionnaire portion of the investigation achieve 25% participation from the retrospective cohort review. Absolute confidentiality was guaranteed to all participants.

Statistical Analysis

Our power calculations indicated that with 242 subjects, our study had an 80% power to detect a statistically significant difference in tumor recurrence with a two sided alpha of 0.05 (see Appendix 1). Our study surpassed that threshold and included 601 patients. Baseline clinical characteristics, tumor data, and survey results from the treatment groups were compared using chi-square analyses, analysis of variance (ANOVA), and Fisher's exact test. These statistical techniques were also employed to compare MMS versus non-MMS treatments. Due to dissimilar follow-up times for patients in the cohort, Cox regression analysis was also performed based on last follow-up date and date of death. The Cox proportional hazards model was utilized to investigate univariate and multivariate associations of risk factors for clinical recurrence of superficial NMSCs. Multivariate models were built through forward stepwise variable addition followed by backward elimination. All statistical analyses were performed using Stata version 12.0 (Stata Corp., College Station, TX).

Institutional Review Board:

The Partners Human Research Committee approved this study.

Student Role:

My role in this project involved participating fully in the creation of the research aims and study design. I assisted in developing the satisfaction questionnaire and formulating the methodology for collecting all data. Prior to submission, I helped draft, review, and revise the IRB proposal. I exclusively performed the data collection, coding, and verification of the electronic medical records. I formulated the tables, tabulated the results, and calculated the frequency values. I performed 100 of the patient questionnaire satisfaction surveys (50% of the total) administered via telephone. With the assistance of my mentor's research coordinator, I employed the statistical software to evaluate the data and assist in the data analysis. Finally, I documented the results and drafted the final report.

RESULTS

The research results section is structured and reported according to the research aims outlined in the introduction (Section 1).

Objective 1:

The Mohs and Dermatologic Surgery Center database search yielded 601 patients with 735 cases of superficial BCC and SCCIS. After medical record review, 15 patients were excluded due to the following reasons: pursuing treatment at an outside institution (2), declining treatment (3), presenting with a recurrence during initial consultation (8), or simultaneously receiving multiple treatment modalities (2). Of the 586 patients remaining, 281 (48.0%) were treated with Mohs micrographic surgery, 214 (36.5%) with topical medications, 55 (9.4%) with cryotherapy, 14 (2.4%) with electrodesiccation and curettage, 13 (2.2%) with observation, 7 (1.2%) with photodynamic therapy, and 2 (0.3%) with excision. Further analysis was limited to patients who received Mohs micrographic surgery [MMS], topical medications [TM] and cryotherapy [CT], leaving 550 patients with 678 tumors in the study cohort. Table 1 summarizes the characteristics of the study cohort stratified by primary treatment modality. The mean age was 70 years and the median follow-up time from superficial NMSC diagnosis was 24 months (range 2-81 months). No difference in age ($p=0.543$), sex ($p=0.181$), immunosuppression ($p=0.694$) or Fitzpatrick skin type ($p=0.762$) was observed between patients treated with MMS, TM, or CT. Immunosuppression was present in 59 (11%) patients owing to organ transplantation ($n=22$), hematological cancers ($n=17$), autoimmune diseases ($n=13$) and other conditions ($n=12$).

Of the tumors included in the study, 227 (33%) were diagnosed as superficial BCC and 451 (67%) as SCCIS. A total of 329 tumors (49%) were treated with MMS, 292 tumors (43%) were treated with TM, and 57 tumors (8%) were treated with CT. Fluoruracil was the most commonly used TM (80%) followed by ingenol mebutate (11%) and imiquimod (9%). A majority of the treated tumors were located in the head and neck region (70%) with an average diameter of 0.8 cm. TM (83%) and CT (91%) were more commonly used to treat SCCIS while MMS (66%) was more commonly used to treat superficial BCC ($p<0.001$). In addition, MMS (66%), TM (76%) and CT (60%) were more commonly used in treating head and neck tumors as compared to tumors located on the arms, hands, trunk, legs, feet and genitalia ($p=0.005$). The diameter of tumors treated via CT (0.6 cm) was slightly smaller than the diameter of tumors treated via MMS (0.8 cm) and TM (0.8 cm) however, this difference was not statistically significant ($p=0.054$).

Objective 2:

Among the 550 patients treated for superficial BCC and SCCIS, there were 11 patients (2%) who experienced clinical recurrences. Details about the individual tumors that recurred are summarized in Table 2. There were 3 patients (0.5%) with recurrent superficial BCCs and 8 patients (1.5%) with recurrent SCCIS. The mean age of this group was 71 years and the majority (63%) was male. Of note, there was one patient who exhibited 3 concomitant recurrences for 3 previously treated superficial BCC lesions. In terms of treatment modalities, 7 (64%) had been treated with TM, 2 with MMS (18%), and 2 with CT (18%). In total, 4 patients (36%) were

immunosuppressed due to inflammatory bowel disease (IBD), rheumatoid arthritis (RA), or organ transplantation. Seven (63%) of the recurrences occurred on the head and neck region. The range of time from treatment to recurrence or incomplete response was 3 to 53 months. The risk of recurrence or incomplete response was significantly higher in patients treated with non-MMS modalities as compared to those treated with MMS (3.3% vs. 0.7%, $p=0.035$).

Objective 3:

Results of univariate and multivariate analysis of possible risk factors associated with clinical recurrence are summarized in Table 3. A total of eight risk factors likely to influence clinical recurrence were analyzed via univariate analysis. On multivariate analysis, only two risk factors independently predicted the risk of clinical recurrence: tumor diameter of 2 cm or higher (HR, 5.9 [95% CI, 1.5-22.1]) and immunosuppression (3.6 [1.0-12.5]).

Objective 4:

Of the 200 patients randomly selected to participate in the satisfaction survey, 142 patients (71%) provided verbal consent. The leading reasons for declining to participate in the telephone survey included lack of time, lack of desire to participate in clinical research, or inability to recall treatment. Characteristics between the survey and study cohort were comparable. In sum, 25% of each study treatment group participated in the satisfaction survey. About 97% of patients who received MMS were satisfied/very satisfied with their treatment versus 91% of patients who received non-MMS treatment ($p=0.092$). While the questionnaire sought responses on treatment satisfaction, patients were also queried about their willingness to undergo their previous treatment option again. Of the patients who participated in the survey, 97% were willing to undergo MMS again. In comparison, 85% of the TM group and 91% of the CT group were willing to undergo those procedures in the future. This preference to undergo MMS again, compared to the non-MMS treatment modalities, was statistically significant ($p=0.014$). Finally, approximately 34% of MMS versus 38% of non-MMS patients were concerned about recurrence ($p=0.309$) (Figure 1).

DISCUSSION

In this single-center retrospective cohort study, individual patient characteristics such as age, sex, immunosuppressive status, and Fitzpatrick skin type were not associated with a particular treatment modality. Instead, our results revealed certain treatment patterns based on tumor diagnosis and location. While MMS was used equally for superficial BCC and SCCIS, non-MMS modalities such as TM and CT were employed more commonly for SCCIS. This variation in treatment may suggest that the majority of superficial BCCs are being identified early, observed, and treated in the clinic setting, rather than being referred for surgical evaluation.

In our study, surgical and non-surgical treatment modalities for epidermally limited NMSC had equivalent efficacy. While MMS was used equally for superficial BCC and SCCIS, non-MMS modalities such as TM and CT were employed more commonly for SCCIS. Still, the most common singular treatment was MMS (49%). A plausible reason is that 70% of the patients exhibited tumors on the head and neck regions, which are traditionally high risk and aesthetically sensitive areas necessitating tissue sparing techniques. Additionally, when confronted with various treatment options, the study's patients may have been more inclined to undergo MMS based on their willingness to be referred to a dermatologic surgeon. Another potential reason may be the preference of dermatologic surgeons to recommend MMS, due to its higher cure rate and treatment completion in one visit, which reduces the need for patient compliance and frequent follow-up.

Notably, the proportion of BCC (33%) and SCCIS (67%) treated in our study were different from previous epidemiological estimates of typical NMSC.^{35,36} Accounting for this difference may be the selection bias of a study cohort consisting of patients with higher risk NMSC, necessitating referral to a surgery center.

While MMS demonstrated a lower recurrence rate (0.7%) than non-MMS treatment modalities (3.3%), this difference was not statistically significant on multivariate Cox regression analysis. High compliance with topical therapy and close follow-up in this cohort may account for the high cure rate of 97%. Accurate risk estimates of outcomes from population-based data and well-controlled clinical trials longer term follow-up are required to further examine treatment efficacy.

Patients with tumor diameter of 2 cm or more and those with compromised immunity were at a significantly higher risk of developing clinical recurrences on multivariate analysis. This finding may offer clinical guidance that for these tumor and patient characteristics, dermatologists should carefully weigh their therapeutic strategies and opt for treatments with a higher cure rate. Examining the underlying reasons for these salient variables should be investigated in future studies.

To assess overall satisfaction, we employed a single global question derived from the satisfaction domain of the Patient Satisfaction Questionnaire-18. This practice has been used before in a long-term satisfaction study of NMSC that focused exclusively on dermatologic surgery, based on the premise that "patients would probably remember overall impressions" after

1 year.³⁴ Additionally, the number of survey questions were limited to minimize completion time for study participants and maximize study participation.

Patient satisfaction did not vary significantly between the treatment groups and overall, a large majority of patients were satisfied with their NMSC treatment. Consequently, although treatment modality can impact patient satisfaction, its effect may not be as profound as previously demonstrated. The results of our survey also established that MMS patients were more willing to undergo the treatment again, which could be interpreted to suggest that MMS patients exhibited some additional degree of underlying satisfaction. In the pre-operative setting, this data may be helpful to counsel patients who are deciding between different treatment options. Finally, a large number of respondents continued to express concern about tumor recurrence. Although the difference in concern for recurrence was not statistically significant between MMS and non-MMS treatment modalities, this data may provide clinical insight into how patients contemplate their treatment afterwards. More importantly, it highlights a discrepancy between actual tumor recurrence rates and patient perception of the risk of recurrence, which highlights an important clinical opportunity to provide patient education and reassurance.

LIMITATIONS

This study is subject to some limitations. The major limitation of this research is its retrospective design. Consequently, patients were not included in a protocol and randomized to different treatment modalities, which is a well-known problem in retrospective studies of treatment. Another limitation was the performance of the study at a single academic center within a geographically unique metropolitan area, which may hinder generalizing the results to other locations. Although the satisfaction survey results demonstrated statistical significance in terms of willingness to undergo certain treatments again; the survey used was not formally validated and as a result, may lack sensitivity. The survey findings also need to be interpreted in the context of the study design. Although patient selection was randomized, the study participants may represent a more motivated and well-informed population. In addition, due to variable follow-up times, the patients may have demonstrated some level of recall bias. Also, since only 25% of the study cohort was included in the satisfaction survey, our data may not be representative of the entire cohort. Future studies should therefore involve a larger, multicenter, prospective trial that evaluates a patient's perspective of their treatment at multiple time points.

CONCLUSIONS

To the best of our knowledge, this is the first study to evaluate efficacy and satisfaction between surgical and non-surgical treatments of NMSC. As healthcare resources become increasingly constrained, our study results suggest that clinicians should recommend higher cure-rate treatment modalities for patients based on tumor size and immunosuppressant status. Furthermore, this study suggests that a large majority of patients are satisfied with their NMSC treatment. Additionally, while Mohs surgery appears to be superior to non-surgical interventions such as TM and CT, in terms of recurrence, the non-invasive treatment options deserve further consideration, based on their efficacy, high patient satisfaction, and lower cost.

SUGGESTED FUTURE WORK

This research contributes relevant insights that may help formulate consensus guidelines for NMCS care and help clinicians optimize treatment strategies based on likelihood of tumor recurrence. Additionally, the results identify clinical opportunities to provide patient reassurance, deliver education, and compare cost effectiveness of surgical versus non-surgical approaches incorporating patient satisfaction. Accurate risk estimates of outcomes from population-based data and well-controlled clinical trials with 2-5 year follow-up are required to further examine treatment efficacy. Additionally, a larger randomized trial may offer additional insights into patient satisfaction, identify clinical opportunities to provide patient reassurance and education, and compare cost-effectiveness of different treatment modalities based on survival.

REFERENCES

1. Rogers HW, Weinstock MA, Harris AR, et al. Incidence estimate of nonmelanoma skin cancer in the United States, 2006. *Arch Dermatol.* 2010; 146(3): 283-287.
2. Arits AH, Schlangen MH, Nelemans PJ, Kelleners-Smeets NW. Trends in the incidence of basal cell carcinoma by histopathological subtype. *Journal of the European Academy of Dermatology and Venereology.* 2011. 25(5): 565-569.
3. Humphreys, TR, Malhotra R, Scharf MJ, Marcus SM, Starkus L, Calegari K. Treatment of superficial basal cell carcinoma and squamous cell carcinoma in situ with a high-energy pulsed carbon dioxide laser. *Arch Dermatol.* 1998. 134(10): 1247-1252.
4. Honeycutt M, Jansen T. Treatment of squamous cell carcinoma of the skin. *Arch Dermatol.* 1973. 108(5): 670- 672.
5. Housman TS, Feldman SR, Williford PM, et al. Skin cancer is among the most costly of all cancers to treat for the Medicare population. *J Am Acad Dermatol.* 2003; 48(3):425–429.
6. Chen JG, Fleischer AB, Smith ED, et al. Cost of nonmelanoma skin cancer treatment in the United States. *Dermatol Surg.* 2001; 27(12): 1035–1038.
7. Glass AG, Hoover RN. The emerging epidemic of melanoma and squamous cell skin cancer. *JAMA.* 1989; 262(15): 2097-2100.
8. Miller DL, Weinstock MA. Non melanoma skin cancer in the US: Incidence. *Journal of American Academy Dermatology.* 1994; 30: 774-778.
9. Green A. Changing patterns in incidence of non-melanoma skin cancer. *Epithelial Cell Biology.* 1992; 1(1): 47-51.
10. Lewis KG, Weinstock MA. Trends in nonmelanoma skin cancer mortality rates in the United States, 1969 through 2000. *J Invest Dermatol.* 2007 127(10): 2323-2327.
11. Guy GP, Machlin SR, Ekwueme DU, Yabroff KR. Prevalence and cost of skin cancer treatment in the U.S., 2002-2006 and 2007-2011. *Am J Prev Med.* 2015 Feb; 48(2):182-187.
12. Chren MM, Sahay AP, Sands LP, et al. Variation in care for nonmelanoma skin cancer in a private practice and a veterans affairs clinic. *Med Care.* 2004; 42(10): 1019–26.
13. Kuijpers D, Thissen M, Neumann M. Basal cell carcinoma: treatment options and prognosis, a scientific approach to a common malignancy. *Am J Clin Dermatol.* 2002; 3(4): 247-259.

14. Neville JA, Welch E, Leffell DJ. Management of nonmelanoma skin cancer in 2007. *Nat Clin Pract Oncol.* 2007; 4(8): 462-9.
15. Bath-Hextall F, Bong J, Perkins W, et al. Interventions for basal cell carcinoma of the skin: systematic review. *BMJ (Clinical research ed.)* 2004; 329(7468): 705.
16. Thissen MR, Neumann MH, Schouten LJ. A systematic review of treatment modalities for primary basal cell carcinomas. *Arch Dermatol.* 1999; 135(10): 1177–1183.
17. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (Basal cell skin cancer and squamous cell skin cancers). June 3, 2011. Available at http://www.nccn.org/professionals/physician_gls/pdf/nmsc.pdf. Accessed November 14, 2014.
18. Wollina U. Update of cetuximab for non melanoma skin cancer. *Expert Opin Biol Ther.* 2014. 14(2): 271-276.
19. Walls B, Jordan L, Diaz L, Miller R. Targeted therapy for cutaneous oncology: a review of novel treatment options for non-melanoma skin cancer: part I. *J Drugs Dermatol.* 2014. 13(8): 947-952.
20. Trost LB, Bailin PL. History of Mohs surgery. *Dermatol Clin.* 2011. 29(2):135-139
21. Patel TN, Patel SB, Franca K, Chacon AH, Nouri K. Mohs micrographic surgery: history, technique, and advancements. *Skinmed.* 2014. 12(5): 289-292.
22. Reeder, VJ, Gustafson CJ, Mireku K, Davis SA, Feldman SR, Pearce DJ. Trends in mohs surgery from 1995-2010: an analysis of nationally representative data. *Dermatol Surg.* 2015. Epub ahead of print.
23. Micali G, Lacarrubba F, Bhatt K, Nasca MR. Medical approaches to non-melanoma skin cancer. *Expert Rev Anticancer Ther.* 2013. 13(12): 1409-21.
24. Goldenberg G, Hamid O. Nonsurgical treatment options for basal cell carcinoma - focus on advanced disease. *J Drugs Dermatol.* 2013; 12(12): 1369-78.
25. Lien MH, Sondak VK. Nonsurgical treatment options for Basal cell carcinoma. *Journal of skin cancer.* 2011; 571734
26. Clark CM, Furniss M, Mackay-Wiggan JM. Basal cell carcinoma: an evidence-based treatment update. *Am J Clin Dermatol.* 2014; 15(3): 197-216.

27. Rosenthal E. Patients' cost skyrockets, specialists' incomes soar. *New York Times*. January 18, 2014; A1.
28. Wilson LS, Pregoner M, Basu R, et al. Fee comparisons of treatments for nonmelanoma skin cancer in a private practice academic setting. *Dermatol Surg*. 2012; 38(4): 570-84.
29. Rogers HW, Coldiron BM. A relative value unit-based cost comparison of treatment modalities for nonmelanoma skin cancer: effect of the loss of the Mohs multiple surgery reduction exemption. *J Am Acad Dermatol*. 2009; 61(1): 96-103.
30. Cook J, Zitelli JA. Mohs micrographic surgery: a cost analysis. *J Am Acad Dermatol*. 1998; 39(5): 698-703.
31. Ravitskiy L, Brodland D, Zitelli J. Cost analysis: Mohs Micrographic Surgery. *Dermatol Surg*. 2012; 38(4): 585-594
32. Essers B, Dirksen C, Nieman F, et al. Cost-effectiveness of mohs micrographic surgery vs surgical excision for basal cell carcinoma of the face. *Arch Dermatol*. 2006; 142(2): 187-194.
33. Renzi C, Abeni D, Picardi A, et al. Factors associated with patient satisfaction with care among dermatological outpatients. *Br J Dermatol*. 2001; 145(4): 617-623.
34. Asgari MM, Warton EM, Neugebauer R, Chren MM. Predictors of patient satisfaction with Mohs surgery: analysis of preoperative, intraoperative, and postoperative factors in a prospective cohort. *Arch Dermatol*. 2011; 147(12): 1387-94.
35. Sharon VR, Armstrong AW, Jim On SC, Ibrahimi OA, Eisen DB. Separate- versus same-day preoperative consultation in dermatologic surgery: a patient-centered investigation in an academic practice. *Dermatol Surg*. 2013; 39(2): 240-7.
36. Sharon VR, Armstrong AW, Jim-On S, Ibrahimi OA, Eisen DB. Postoperative preferences in cutaneous surgery: a patient-centered investigation from an academic dermatologic surgery practice. *Dermatol Surg*. 2013; 39(5): 773-8.
37. Asgari MM, Bertenthal D, Sen S, Sahay A, Chren MM. Patient satisfaction after treatment of nonmelanoma skin cancer. *Dermatol Surg*. 2009; 35(7): 1041-1049

TABLES AND FIGURES

Table 1. Cohort Characteristics Stratified by Treatment Modality

Characteristic	Total	MMS	TM	CT	p value*
	n (%)	n (%)	n (%)	n (%)	
Total no. of patients	550	281 (51)	214 (39)	55 (10)	--
Age, years					
Mean (SD)	70 (13)	68 (14)	70 (13)	75 (13)	0.543 [†]
Sex					
Male	276 (50)	142 (51)	99 (46)	33 (60)	0.181
Female	274 (50)	139 (49)	115 (54)	22 (40)	
Immunosuppression					
No	491 (89)	248 (88)	194 (91)	49 (89)	0.694
Yes	59 (11)	33 (12)	20 (9)	6 (11)	
Reason for Immunosuppression					
Organ transplant	22 (37)	12 (36)	8 (40)	2 (33)	0.633
Leukemia/lymphoma	17 (29)	11 (33)	3 (15)	3 (50)	
Autoimmune diseases	13 (22)	6 (18)	6 (30)	1 (17)	
Other	7 (12)	4 (13)	3 (15)	0 (0)	
Fitzpatrick skin type					
I	111 (20)	56 (20)	42 (20)	13 (24)	0.762
II	179 (32)	87 (31)	73 (34)	19 (35)	
III	208 (38)	113 (40)	78 (36)	17 (31)	
IV	34 (6)	18 (7)	10 (5)	6 (10)	
V	6 (1)	3 (1)	3 (1)	0 (0)	
VI	3 (1)	1 (0)	2 (1)	0 (0)	
Unknown	9 (2)	3 (1)	6 (3)	0 (0)	

Table 1 (continued). Cohort Characteristics (Continued)

Characteristic	Total n (%)	MMS n (%)	TM n (%)	CT n (%)	p value*
Total no. of tumors	678	329 (49)	292 (43)	57 (8)	--
Tumor diagnosis					
Superficial BCC	227 (33)	171 (52)	51 (17)	5 (9)	
SCC in situ	451 (67)	158 (48)	241 (83)	52 (91)	<0.001
Tumor location					
Head/neck (including ear/lip)	473 (70)	217 (66)	222 (76)	34 (60)	
Arms, hands, trunk, genitalia, legs, feet	205 (30)	112 (34)	70 (24)	23 (40)	0.005
Tumor diameter, cm					
Mean (SD)	0.8 (0.6)	0.8 (0.6)	0.8 (0.6)	0.6 (0.4)	0.054 [†]
< 2.0	626 (92)	313 (95)	257 (88)	56 (98)	
≥ 2.0	36 (5)	16 (5)	19 (7)	1 (2)	
Unknown	16 (3)	0 (0)	16 (5)	0 (0)	0.279 [‡]

Abbreviations: Mohs micrographic surgery (MMS), topical medications (TM), cryotherapy (CT), and standard deviation (SD);

*Based on Chi² statistics unless otherwise specified; [†]Analysis of variance (ANOVA); [‡]Fisher's exact test.

Table 2. Characteristics of Patients that had Recurrence or Incomplete Treatment Response During the Study Period

ID	Age	Sex	Diagnosis	Tumor Location	Treatment	Immunosuppression (Reason)	Time to Recurrence/ Incomplete Response
1	80	Male	SCC in situ	Head/neck	MMS	No	21 months
2	60	Male	SCC in situ	Arms/hand	MMS	Yes (IBD)	10 months
3	71	Male	Superficial BCC	Legs/feet	TM	No	5 months
4	70	Male	SCC in situ	Head/neck	TM	No	29 months
5	75	Female	SCC in situ	Head/neck	TM	Yes (RA)	53 months
6	81	Male	SCC in situ	Head/neck	TM	Yes (OTR)	25 months
7	57	Female	SCC in situ	Arms/hand	TM	No	18 months
8	74	Female	SCC in situ	Head/neck	TM	No	3 months
9	87	Male	Superficial BCC	Legs/feet	TM	Yes (OTR)	4 months
10	54	Male	Superficial BCC	Head/neck	CT	No	12 months
11	74	Female	SCC in situ	Head/neck	CT	No	18 months

Abbreviations: Mohs micrographic surgery (MMS), Topical medications (TM), Cryotherapy (CT), Squamous cell carcinoma (SCC), Basal cell carcinoma (BCC),

Inflammatory bowel disease (IBD), Rheumatoid arthritis (RA), Organ transplant recipient (OTR).

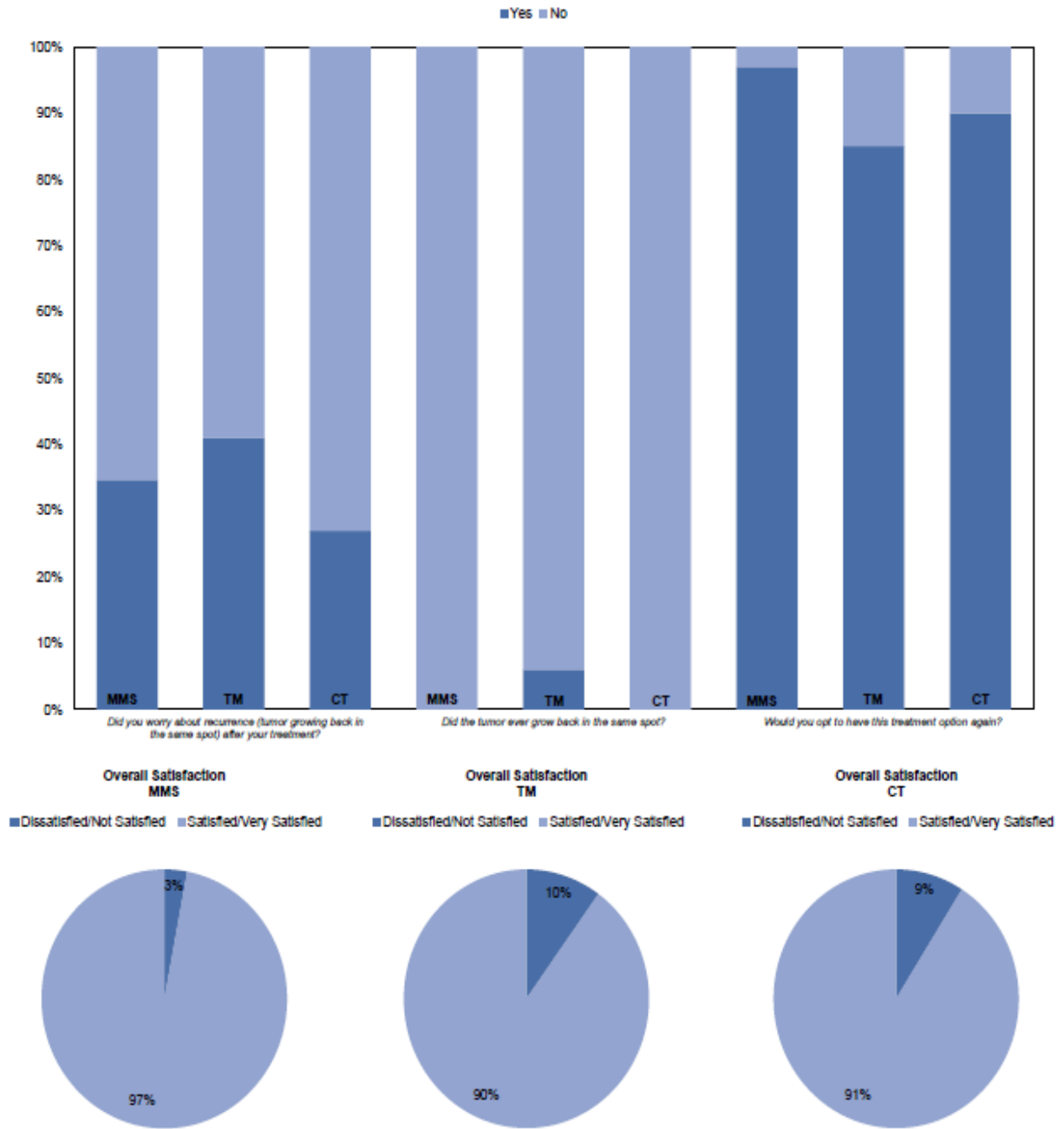
MMS vs. TM incomplete response: 0.7% (2/281) vs. 3.3% (7/214), p=0.035 *statistically significant* \\ MMS vs. CT incomplete response: 0.7% (2/281) vs. 3.6% (2/55), p=0.067 *approaching statistical significance* \\ CT vs. TM incomplete response: 3.6% (2/55) vs. 3.3% (7/214), p=0.893 *not statistically significant*

Table 3. Factors Associated with Recurrence or Incomplete Treatment Response

Variable	Univariate Analysis		Multivariate Analysis	
	HR (95% CI)	p value	HR (95% CI)	p value
Age, 1 yr increase	1.0 (0.9-1.1)	0.774	--	--
Gender				
Female	1.0			
Male	1.9 (0.6-6.5)	0.310	--	--
Tumor diagnosis				
Superficial BCC	1.0			
SCC in situ	0.9 (0.2-3.5)	0.907	--	--
Tumor diameter				
< 2.0 cm	1.0			
≥ 2.0 cm	5.9 (1.5-22.1)	0.009	5.1 (1.3-19.5)	0.018
Tumor location				
Other	1.0			
Head/neck (including ear and lip)	0.7 (0.2-2.5)	0.601	--	--
Immunosuppression status				
No	1.0			
Yes	2.8 (0.7-10.4)	0.134	3.6 (1.0-12.5)	0.042
Treatment				
Mohs	1.0			
Topical medications and cryotherapy	4.0 (0.9-18.5)	0.077	--	--
Post-treatment complications				
No	1.0			
Yes	3.2 (0.7-14.7)	0.141	--	--

Abbreviations: Hazards ratio (HR), Confidence interval (CI), Centimeters (CM).

Figure 1. Results of the Patient Satisfaction Survey Stratified by Treatment Modality. MMS: Mohs micrographic surgery, TM: topical medications and CT: cryotherapy.



Opt to have treatment again: MMS (97%) vs. TM (85%) vs. CT (91%), $p=0.069$ *approaching statistical significance*

APPENDICES

Appendix 1. Power Calculations

Mohs vs. Other Treatment Trends for Superficial BCC/SCC In Situ 2008-2013

Time Period	Mohs Surgery (%)	Other Treatment (%)
01/2008-06/2008	9 (26%)	25 (74%)
07/2008-12/2008	15 (31%)	33 (69%)
01/2009-06/2009	14 (34%)	27 (66%)
07/2009-12/2009	17 (47%)	19 (53%)
01/2010-06/2010	18 (34%)	35 (66%)
07/2010-12/2010	18 (34%)	35 (66%)
01/2011-06/2011	19 (30%)	44 (70%)
07/2011-12/2011	12 (16%)	61 (84%)
01/2012-06/2012	28 (38%)	46 (62%)
07/2012-12/2012	37 (45%)	45 (55%)
01/2013-06/2013	39 (44%)	49 (54%)
07/2013-12/2013	86 (66%)	44 (34%)

Power Analysis

Sample Size: X-Sectional, Cohort, & Randomized Clinical Trials

Two-sided significance level(1-alpha):	95
Power(1-beta, % chance of detecting):	80
Ratio of sample size, Unexposed/Exposed:	1
Percent of Unexposed with Outcome:	10
Percent of Exposed with Outcome:	0.99
Odds Ratio:	0.09
Risk/Prevalence Ratio:	0.1
Risk/Prevalence difference:	-9

	Kelsey	Fleiss	Fleiss with CC
Sample Size - Exposed	101	100	121
Sample Size-Nonexposed	101	100	121
Total sample size:	202	200	242

Appendix 2. Introductory Study Letter



BRIGHAM AND
WOMEN'S HOSPITAL

DANA-FARBER/BRIGHAM AND WOMEN'S



CANCER CENTER



HARVARD
MEDICAL SCHOOL

April 7, 2015

Dear Sir/Madame,

I am contacting you because you have previously received treatment for superficial skin cancer at the Mohs and Dermatologic Surgery Center at Brigham and Women's Faulkner Hospital. I would like to ask you to consider participating in a patient satisfaction survey that I am conducting as part of a research study. The satisfaction survey is not from the hospital, it is for research purposes only.

The purpose of the survey is to determine if differences exist in patient satisfaction by type of treatment modality. The survey is part of a larger study that will be evaluating treatment patterns for patients diagnosed with superficial skin cancer. The survey will be administered via the telephone and your expected time commitment to answer the questions is five minutes. You may skip any questions you do not wish to answer. A total of 200 patients will participate in this survey. We will also be storing some of your health information with the survey. We will review your medical records to collect details from the treatment(s) you received so that we can accurately describe traits of the group of patients who participate in this research study.

You will not be identified by name in any reports using information obtained from this survey. Your personal information will remain private and will not be shared with anyone. My research staff will contact you by telephone in about one week to see if you are interested in participating in this survey. Your participation is voluntary and you will not be paid for your participation. Your decision to participate will not change the medical care you receive within Partners now or in the future.

We are required by the Health Insurance Portability and Accountability Act (HIPAA) to protect the privacy of health information obtained for research. This is an abbreviated notice, and does not describe all details of this requirement. During this research study, identifiable information about you or your health will be collected and shared with the researcher conducting the research. In general, under federal law, identifiable health information is private. However, there are exceptions to this rule. In some cases, others may see your identifiable health information for purposes of research oversight, quality control, public health and safety, or law enforcement. We share your health information only when we must, and we ask anyone who receives it from us to protect your privacy.

If you have any questions or need more information about this research study, please feel free to contact me during weekdays at (617) 983-4626 or my research coordinator Pritesh Karia, MPH at (617) 983-7207. If you want to speak with someone not directly involved in this research study, please contact the Partners Human Research Committee at (617) 424-4100.

Sincerely,

Chrysalyn D. Schmults, MD, MSCE

Director, Mohs and Dermatologic Cancer Center
Dana-Farber/Brigham and Women's Cancer Center
Department of Dermatology, Brigham and Women's Hospital

Member of PARTNERS HealthCare

Appendix 3. Patient Satisfaction Questionnaire/Telephone Script

Good morning/good afternoon my name is _____ and I'm calling from the Mohs and Dermatologic Surgery Center at the Brigham and Women's Faulkner Hospital. I'm a researcher working with Dr. Chrys Schmults and I'm calling about the treatment you had for the basal cell/squamous cell carcinoma on your _____ (tumor location) on _____ (date of treatment). We're conducting a research study to determine if patients are satisfied with their treatment. We sent you a letter informing that we would call you. Did you receive the letter?

- **No.** Would you like us to send you another letter?
- **Yes.** Thank you.

Do you have two minutes to answer a few questions?

- **No.** Is there a convenient time I can call you back?
 - If patient **declines** to participate: Thank you very much for your time.
- **Yes.** Thank you. The purpose of the survey is to determine whether patients are satisfied with the surgery they received. The satisfaction survey is not from the hospital, it is for research purposes only. You may skip any questions you do not wish to answer. We will also be storing some of your health information with the survey so we can accurately describe traits of the group of patients who participate in this survey. You will not be identified by name in any reports using information obtained from this survey and your personal information will not be shared with anyone.

1. Do you remember having the basal cell/squamous cell carcinoma treated on your _____ (tumor location) in _____ (month/year)?

2. Overall, how satisfied are you with your treatment?

- Very Satisfied
- Satisfied
- Not Satisfied
- Very Dissatisfied

3. Did you worry about recurrence (tumor growing back in the same spot) after your treatment?

- Yes
- No

4. Did the tumor ever grow back in the same spot?

- Yes
- No

5. Would you opt to have this treatment option again?

- Yes
- No

6. Is there anything else you would like us to know about your recovery after your treatment?