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Seasonal and Geographic Trends in Photodynamic Therapy and Cryosurgery Use in the United States: A Cross-sectional Study From 2015-2022

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BACKGROUND: Photodynamic therapy (PDT) is an effective field treatment for actinic keratoses (AKs). It is an ideal option for patients who prefer a minimally invasive procedure conveniently administered in their physician's office. Anecdotal clinician insights suggest that it may not be used at the same rate year-round. **OBJECTIVE:** This study investigates whether PDT and cryosurgery usage is affected by season and geographic location in the United States. **METHODS:** The data source is an aggregate of closed and open United States medical procedural claims (*Common Procedural Code* [CPT] and Healthcare Common Procedure Coding System [HCPCS]) from a broad selection of commercial payers and Centers for Medicare & Medicaid Services (CMS) from 2015 to 2022. Patient records associated with cryosurgery and PDT CPT codes were extracted. A total of 79.1 million patients from 50 states and 4 territories between 2015 to 2022 were included in the analysis. The data were further stratified using meteorologically defined seasons and geographic locations. **RESULTS:** PDT utilization is affected by season and geographic location. Procedural claims peak during cooler months and decrease during warmer months, particularly where seasonal changes are more drastic. This trend repeats throughout the study period, including the COVID-19 pandemic. In contrast, use of cryosurgery remains unchanged. **LIMITATIONS:** The dataset does not capture claims from all commercial payers and CMS. **CONCLUSION:** To our knowledge, this study provides the first evidence of PDT seasonal usage patterns across the nation. This pattern could be attributed to several factors and the findings could serve as a learning opportunity for clinicians to reevaluate their approach in treating AKs. **KEYWORDS:** Actinic keratosis, photodynamic therapy, PDT, cryosurgery, procedural claims, CMS, seasonality, real-world evidence

Actinic keratosis (AK) is one of the most common skin conditions treated by dermatologists in the United States (US), with AKs diagnosed in more than 10% of outpatient dermatology visits and reported in up to 26% of Americans aged 30 years or older.^{1,2} Early detection and treatment of AK is important, as the lesions can progress into cutaneous squamous cell carcinomas (cSCCs), the second most common type of nonmelanoma skin cancers (NMSC). Because of its high prevalence and potential for malignant transformation, AK is an important health concern and presents a financial impact on the healthcare system. In 2013, the estimated cost of treating AK in the US was \$1.68 billion,³ while the annual cost of treating nonmelanoma skin cancers (NMSCs) was estimated at \$4.8 billion from 2007 to 2011.⁴

There are multiple treatment options available for the management of AK in the US, including cryosurgery, topicals, and photodynamic therapy (PDT), and while there isn't a universally established standard of care, cryosurgery has long been a first-line option due to its ease of in-office administration and reported efficacy.^{5,6} Cryosurgery, however, can only be performed in a lesion-directed manner and is therefore not suitable for addressing field cancerization. It is also associated with potential adverse effects, such as blistering, long-term scarring, and hypopigmentation.⁵ PDT is an in-office, light/energy-based treatment that offers a noninvasive approach to AK treatment. PDT has some of the highest reported clearance rates, including sustainable long-term efficacy at 12 months, and is associated with enhanced cosmetic outcomes

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TABLE 1. Descriptions for each CPT code used in this study

CPT CODE	DESCRIPTION
17000	Destruction (eg, laser surgery, electrosurgery, cryosurgery, chemosurgery, surgical curettement), premalignant lesions (eg, actinic keratoses); first lesion
17003	Destruction (eg, laser surgery, electrosurgery, cryosurgery, chemosurgery, surgical curettement), premalignant lesions (eg, actinic keratoses); second through fourteenth lesions, each (list separately in addition to code for first lesion)
17004	Destruction (eg, laser surgery, electrosurgery, cryosurgery, chemosurgery, surgical curettement), premalignant lesions (eg, actinic keratoses), 15 or more lesions
96567	PDT by external application of light to destroy premalignant and/or malignant lesions of the skin and adjacent mucosa (eg, lip) by activation of photosensitive drug(s), each phototherapy exposure session
96573	PDT by external application of light to destroy premalignant lesions of the skin and adjacent mucosa with application and illumination/activation of photosensitizing drug(s) provided by a physician or other qualified health care professional, per day
96574	Debridement of premalignant hyperkeratotic lesion(s) (ie, targeted curettage, abrasion) followed with PDT by external application of light to destroy premalignant lesions of the skin and adjacent mucosa with application and illumination/activation of photosensitizing drug(s) provided by a physician or other qualified health care professional, per day

PDT: photodynamic therapy

and high patient satisfaction.⁷⁻¹² The biggest advantage of PDT is that it can be performed in a field-directed manner in which individual visible lesions as well as subclinical damage are treated simultaneously. This addresses field cancerization, which helps minimize the recurrence of AK lesions and could arguably help prevent their potential progression to cSCC¹²⁻¹⁵—though long-term studies are yet to be conducted to conclusively show a prophylactic effect of PDT. In addition, PDT has shown very good short- and long-term efficacy for the treatment of basal cell carcinoma (BCC) and Bowen's disease (SCC in situ [SCCis]).^{7,12,16-19} While approved in Europe, PDT is still off-label for the treatment of NMSC in the US.^{20,21} The

TABLE 2. Gender difference in claims for cryosurgery and PDT during each season from 2015 to 2022

SEASON	CRYOSURGERY CLAIMS				PDT CLAIMS			
	FEMALE	MALE	UNKNOWN	TOTAL	FEMALE	MALE	UNKNOWN	TOTAL
Winter	7,086,872	11,249,511	4214	18,340,597	137,920	208,411	89	346,420
Spring	7,583,590	11,568,934	4170	19,156,694	113,835	159,395	71	273,301
Summer	7,769,603	12,294,108	4662	20,068,373	71,253	104,912	60	176,225
Fall	8,037,839	12,425,229	4405	20,467,473	121,949	173,886	69	295,904
Total	30,477,904 (39.1%)	47,537,782 (60.9%)	17,451 (0.0%)	78,033,137	444,957 (40.8%)	646,604 (59.2%)	289 (0.0%)	1,091,850

major adverse effect of PDT is pain during treatment, and there are many practical pain management strategies to help improve patient comfort.²¹ In addition, recent studies and protocol amendments have sought to decrease patient discomfort by either reducing the incubation time of the aminolevulinic acid (ALA) or using daylight or artificial daylight as a light source, essentially using a light source with decreased energy fluence while increasing the illumination duration to activate the photosensitizer.^{22,23}

PDT received Medicare coverage for the treatment of AK in 2001, which provided millions of Americans with an additional in-office and cost-effective therapy to treat lesions and help mitigate their risk of progression to cSCC.^{24,25} With 29.3% of Medicare beneficiaries receiving at least one AK diagnosis between 2009 and 2018, and an estimated 72% of cSCCs originating from preexisting AKs, the need for efficacious and cost-effective treatments is dire.^{26,27} PDT has been shown to be one of the most cost-effective in-office treatments, thus increasing its implementation footprint and frequency could help alleviate the growing healthcare burden associated with AK and NMSCs in the US.^{3,28,29}

Although the efficacy of PDT is well documented in numerous published studies, anecdotal clinician insights suggest that it may not be used at the same rate year-round and that this "PDT seasonality" may vary by geographic location. In contrast, this seasonal trend has not been observed or reported with cryosurgery. This study aims to analyze PDT usage patterns as compared to cryosurgery to investigate whether PDT use is affected by season and geographic location in the US. The findings will provide insights on physician behavior and a learning opportunity for better use of PDT across the nation that would capitalize on the advantages offered

to patients and the healthcare system year-round.

METHODS

The data source is an aggregate of closed and open US medical procedural claims (*Common Procedural Code [CPT]* and *Healthcare Common Procedure Coding System [HCPCS]*) from a broad selection of commercial payers and Centers for Medicare and Medicaid Services (CMS) from 2015 to 2022. Patient records associated with CPT codes 17000, 17003, and 17004 for cryosurgery and 96567, 96573, and 96574 for PDT were extracted. A total of 79.1 million patients from 50 states and 4 territories between 2015-2022 were included in the analysis. The descriptions for each CPT code can be found in Table 1.

The results were further stratified based on meteorologically defined seasons: December 1 to February 28 (winter), March 1 to May 31 (spring), June 1 to August 31 (summer), and September 1 to November 30 (fall). Sinusoidal regression in the datasets was used to determine whether seasonality exists in the administration of cryosurgery and PDT in the US. Due to the impact of the COVID-19 pandemic, particularly on the administration of in-office procedures, data from the year 2020 were considered outliers and were excluded from the analysis.

RESULTS

Of the 79.1 million patient records analyzed from 2015 to 2022, the majority were men, accounting for 60.9% of cryosurgery claims and 59.2% of PDT claims (Table 2). Patients aged 65 to 88 years accounted for the highest number of claims for both cryosurgery and PDT, closely followed by those aged 45 to 64 years (Table 3; Figure 1). Cryosurgery claim numbers peaked in the fall while PDT claims peaked in the winter (Table 3). Florida, California, Texas, and New York

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were the top four states with the highest number of procedural claims for both cryosurgery and PDT between 2015 and 2022 (Figure 2).

There was an increase in cryosurgery claims from 2015 to 2017, after which they stabilized. A significant decline in claims was observed in April 2020, aligning with the impact of COVID-19 pandemic lockdowns that restricted office visits that year. As such, all data from 2020 were excluded from the seasonality regression analysis. Despite slight monthly variations in claims, data analysis revealed no statistically significant seasonal trend in cryosurgery procedural claims ($p=0.61$) (Figure 3A). In contrast, PDT procedural claims showed cyclical seasonality, significantly increasing during the cooler months, with a peak around November and December, and decreasing during the warmer months, particularly around July ($p=0.0000159$) (Figure 3B). This seasonal pattern recurred annually from 2015 to 2022.

When comparing procedural claims from winter (December to February) and summer months (June to August) across the US, cryosurgery claims exhibited minimal differences across geographic locations (Figure 4A). In contrast, PDT claims display differences of up to 278% in winter months compared to summer months (Figure 4B). These variations are particularly pronounced in northern states such as North Dakota, South Dakota, Montana, Nebraska, Minnesota, Iowa, Wisconsin, and New Hampshire. Conversely, southern states including California, Arizona, Nevada, Louisiana, and Florida exhibited the least amount of change in claims between winter and summer months.

Throughout all seasons from 2015 to 2022, men consistently accounted for the majority of claims for both PDT and cryosurgery concerning premalignant skin lesions, and most claims were made by patients aged 45 and 88 years (Table 2, Figure 1). Both results are expected due to the higher prevalence of AK in men and elderly patients.^{2,30,31}

DISCUSSION

This is the first time that seasonal trends in PDT and cryosurgery in the US were studied, with evidence provided on the disparity in PDT utilization across the US. Our data showed that there was no significant treatment seasonality for cryosurgery treatments, with minimal differences in claims between cooler and warmer months across the different states (Figure 3A, Figure 4A). In contrast, there was

TABLE 3. Age disparity in claims for cryosurgery and PDT during each season from 2015 to 2022

AGE GROUP (YEARS)	CRYOSURGERY CLAIMS, n (%)				
	WINTER	SPRING	SUMMER	FALL	TOTAL
<18	43,964 (21.4)	47,919 (23.4)	61,826 (30.1)	51,368 (25.0)	205,077
18–44	245,468 (22.4)	270,093 (24.7)	306,071 (27.9)	273,588 (25.0)	1,095,220
45–64	3,670,758 (23.7)	3,724,869 (24.1)	3,959,443 (25.6)	4,126,706 (26.7)	15,481,776
65–88	12,413,509 (23.5)	12,951,101 (24.5)	13,554,604 (25.7)	13,873,702 (26.3)	52,792,916
≥89	1,966,105 (23.3)	2,161,797 (25.6)	2,185,431 (25.8)	2,141,208 (25.3)	8,454,541
N/A	793 (22.0)	915 (25.4)	998 (27.7)	901 (25.0)	3607
Total	18,340,597	19,156,694	20,068,373	20,467,473	78,033,137

AGE GROUP (YEARS)	PDT CLAIMS, n (%)				
	WINTER	SPRING	SUMMER	FALL	TOTAL
<18	153 (25.5)	151 (25.2)	146 (24.4)	149 (24.9)	599
18–44	9046 (26.8)	7462 (22.1)	7830 (23.2)	9407 (27.9)	33,745
45–64	95,209 (33.3)	68,938 (24.1)	42,022 (14.7)	79,724 (27.9)	285,893
65–88	228,242 (31.7)	183,223 (25.4)	115,806 (16.1)	193,467 (26.8)	720,738
≥89	13,769 (27.1)	13,525 (26.6)	10,416 (20.5)	13,154 (25.9)	50,864
N/A	1 (9.1)	2 (18.2)	5 (45.5)	3 (27.3)	11
Total	346,420	273,301	176,225	295,904	1,091,850

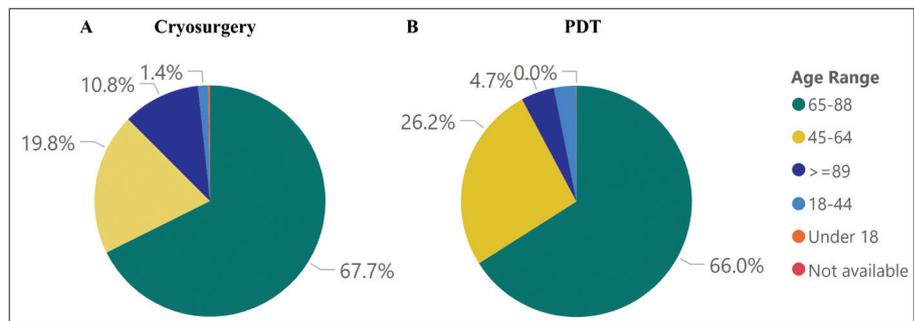


FIGURE 1. Patients stratified by age for (A) cryosurgery and (B) photodynamic therapy (PDT) claims from 2015 to 2022

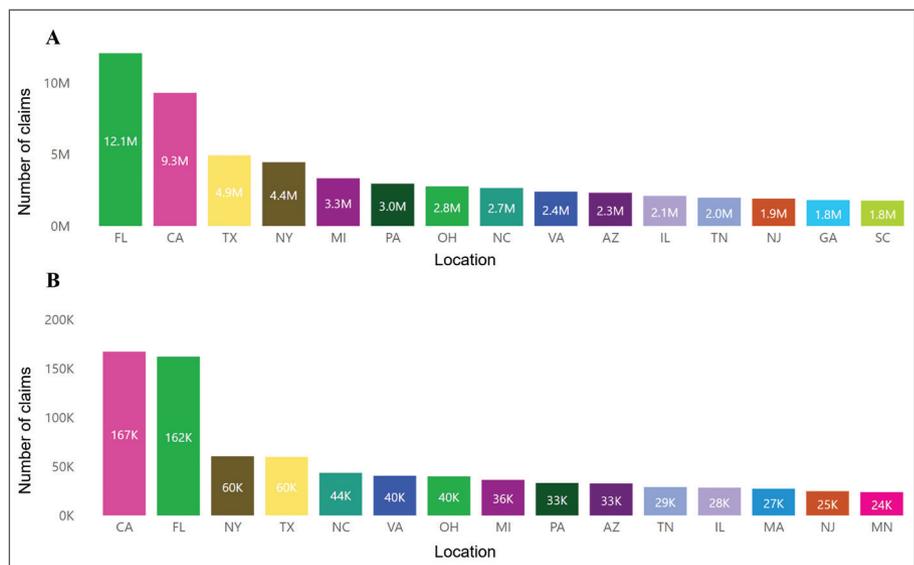


FIGURE 2. Top 15 states by (A) cryosurgery and (B) photodynamic therapy (PDT) procedural claims from 2015 to 2022

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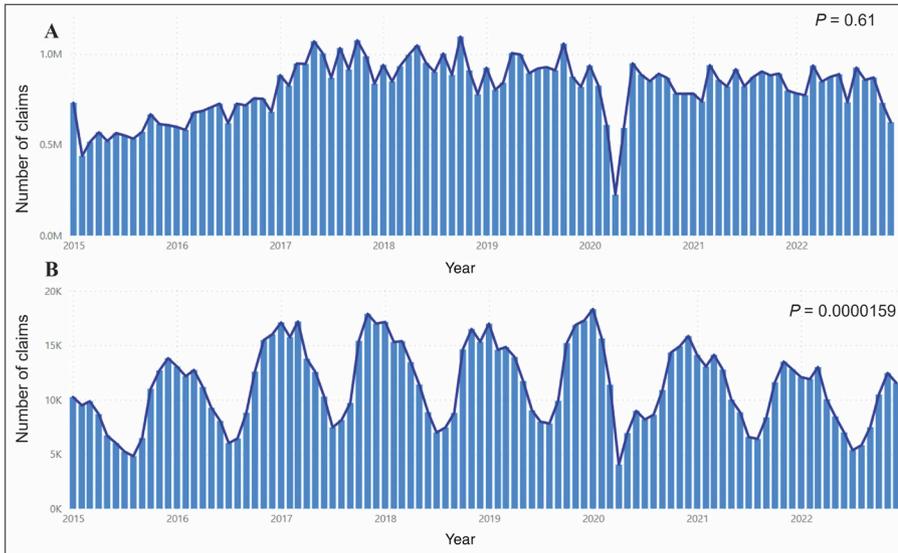


FIGURE 3. Number of (A) cryosurgery procedural claims and (B) photodynamic therapy (PDT) procedural claims in the continental United States per month from 2015 to 2022. *P* values were calculated through sinusoidal regression. Analysis excluded data from 2020 due to the COVID-19 pandemic

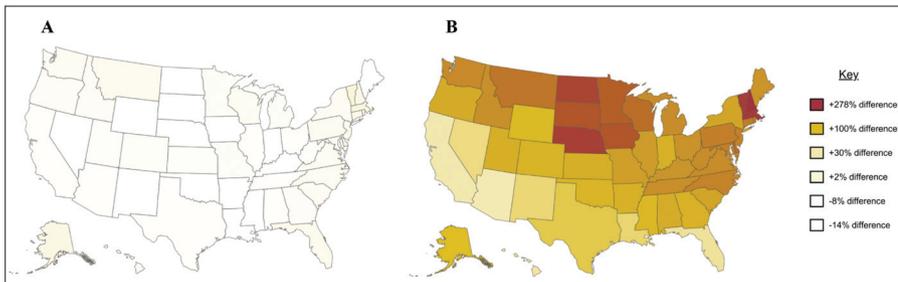


FIGURE 4. Percentage difference in (A) cryosurgery procedural claims and (B) PDT procedural claims during winter compared to summer, stratified by geographic location from 2015 to 2022

a cyclical seasonality with winter peaks and summer lows that persisted for PDT from 2015 to 2022 (Figure 3B, Figure 4B). When PDT claims are compared between winter and summer across the US, warmer states with fewer fluctuations in weather throughout the year, such as California, Arizona, New Mexico, Texas, Louisiana, and Florida, exhibited the least change in PDT claim numbers between the two seasons (Figure 4B).³² However, states with significant temperature variations throughout the year that also experience colder winters showed the most considerable differences in the number of PDT procedures between winter and summer.³²

Multiple factors could be attributed to the observed seasonality in PDT administration. Many physicians recommend undergoing dermatologic treatments, including PDT, in the winter months to avoid complications

due to sun exposure in the typically sunnier summer months and due to patients wearing lighter, less sun-protective clothing.³³ People tend to engage more in outdoor activity during the summer months, and PDT safety protocol involves patients avoiding sunlight and artificial UV exposure for 40 to 48 hours post-procedure due to the increased photosensitivity experienced post-treatment.³⁴ Individuals residing in northern states may opt to maximize outdoor activities or vacations in the summer, hence preferring to undergo PDT in the winter. Also, there typically is an increase in social activities, such as weddings, outdoors gatherings, concerts, and travel, during the summer months, and the adverse effects of PDT (eg, erythema, swelling, scaling) on the treated area might deter people from getting this therapy during the busiest social season of the year.

PDT holds an advantage over cryosurgery because it offers a field-directed approach that targets field cancerization and multiple AKs on sun-damaged skin without the long-term adverse effects attributed to cryosurgery (eg, scarring and hypopigmentation). This makes it a desirable treatment option for cosmetically sensitive areas such as the face and the hands. Furthermore, a recent review focusing on the efficacy, cost, and adherence of the various field-directed therapies for AK determined PDT to be the most cost-effective treatment along with 4% 5-fluorouracil (5-FU) and stipulated that the high patient adherence of PDT would provide an added advantage in its improved real-world efficacy and long-term clearance.²⁸ In fact, the tolerability profile of PDT makes it a strong central player in the network of AK treatments since it can be combined with other available AK therapies and benefit patients who have received treatments limited to target lesions, such as cryosurgery, or who have failed previous monotherapies.³⁵ Considering these advantages, a restricted use of PDT could lead to reduced benefits for both patients and the healthcare system, while administering PDT year-round may optimize patient outcomes and mitigate the economic impact on a financially strained healthcare system.

Physicians can overcome barriers to treatment in the summertime by implementing simple tactics such as picking a favorable day of the week and working around their patients' planned activities when scheduling PDT sessions. They can provide detailed post-treatment care instructions, emphasizing the use of protective measures, such as a tinted sunscreen and protective gear, to shield from UV and daylight exposure. Additionally, it is important to properly counsel patients about the risks of not following these UV safety measures to effectively minimize adverse events. While especially helpful in the summer months, these tactics are applicable and beneficial any time that PDT is administered.

CONCLUSION

Despite its well-documented efficacy and safety as a year-round treatment for AK, our study shows that PDT is underutilized during the summer season, particularly in northern states. Anecdotal insights gathered from healthcare professionals implied the existence of such seasonality in PDT use. Our findings could

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serve as a learning opportunity for clinicians to reevaluate their approach in treating AKs and to implement PDT as a year-round treatment in practice, either alone or in combination with other AK treatments (including cryosurgery) because of the advantages it offers to the affected patient population and the healthcare system as an efficacious, cost-effective, field-directed treatment. There is an overarching need for education on the practical implementation of PDT for the benefit of HCPs and patients alike. Future studies should seek to bridge gaps in the existing clinical practices and published guidelines³⁶ and to provide real-world recommendations for improving use of this therapy.

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